Cartilage Tumors: Evaluation and Treatment

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Abstract

The proper treatment of cartilaginous tumors is dependent on the clinicopathologic and radiologic findings. Enchondroma is a benign tumor that is usually asymptomatic and thus should be treated nonoperatively. Symptomatic enchondromas are often treated by intralesional excision. Intramedullary low-grade chondrosarcoma is a malignant tumor that is usually painful. The treatment of low-grade chondrosarcoma may range from intralesional excision with or without adjuvant therapy to wide excision. Although intralesional excisions have a higher bone and joint preservation rate than wide excisions, they may be associated with a higher local recurrence rate. Intermediate- and high-grade chondrosarcomas are treated with wide excisions. The treatment of these cartilaginous lesions should involve a multidisciplinary team including a musculoskeletal surgeon, a radiologist, and a pathologist.

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Cartilaginous neoplasms are relatively common tumors that can involve almost any bone.[1] These tumors vary in presentation and can range from a latent enchondroma to a high-grade or dedifferentiated chondrosarcoma. The major dilemma facing the surgeon is clinically and radiologically differentiating an enchondroma from a low-grade chondrosarcoma. Occasionally, even the histologic diagnosis can be difficult. The diagnosis and treatment options for these tumors are dependent on a combination of clinical, radiologic, and histologic findings.

Most musculoskeletal surgeons, radiologists, and pathologists can readily distinguish an enchondroma from a high-grade chondrosarcoma. Enchondromas are benign intramedullary tumors that are usually asymptomatic and do not metastasize.[1] They are most commonly located in the short tubular bones in the hands but are also found in long bones. Radiographs usually demonstrate a small (<5 cm) cartilaginous lesion with intramedullary calcifications without cortical involvement or soft-tissue extension.[1-4] Histologically, enchondromas exhibit discrete islands of hyaline cartilage surrounded by lamellar bone. Multinucleated cells are rare. An asymptomatic enchondroma usually does not require treatment beyond observation. Occasionally, symptomatic enchondromas are treated by intralesional excision. The incidence of local recurrence is extremely low.[4]

High-grade chondrosarcomas are malignant neoplasms that commonly recur and metastasize.[5-9] This tumor is usually painful and often demonstrates a range of radiographic findings, including cortical destruction, significant endosteal scalloping, cortical thickening, and soft-tissue extension. High-grade chondrosarcomas are characterized by marked atypia, mitotic figures, and some spindle elements. A wide excision is necessary to obtain local control of these tumors.

Enchondromas and high-grade chondrosarcomas have distinct clinicopathologic and radiologic appearances, which can be used to easily distinguish one entity from the other. However, enchondromas and intramedullary low-grade chondrosarcomas of long bones can resemble each other clinically, radiologically, and histologically. Intramedullary low-grade chondrosarcomas are usually painful. They are most commonly located in the metaphyses of the humerus, femur, or tibia and are usually larger (>5 cm) than an enchondroma. Endosteal scalloping and lysis are common.[2,10] Cortical thickening, expansion, or disruption and soft-tissue masses are uncommon findings.[10,11] Because low-grade chondrosarcomas can have cytologic features similar to those of enchondromas, histologic evaluation is important.[12,13]

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Low-grade chondrosarcomas rarely metastasize, but frequently recur if inadequate surgery is performed.[7-9] Most authors therefore recommend a wide excision to eradicate a low-grade chondrosarcoma, although some have advocated intralesional therapy. Wide excisions are associated with low local recurrence rates, whereas intralesional excisions are associated with high local recurrence rates. Intralesional excisions combined with adjuvant therapy, however, are associated with low mortality and local recurrence rates in carefully selected patients with low-grade chondrosarcomas.[14] Intralesional excisions preserve the adjacent bone and joint surfaces, which probably improves the functional outcome. The primary dilemma is determining which intramedullary low-grade chondrosarcomas can be treated by intralesional excision rather than wide excision. A thorough evaluation of the clinical presentation, radiographic findings, and histologic appearance is necessary to determine the most appropriate treatment (Table 1).

Clinical Presentation

Enchondroma involving a metacarpal or phalanx of the hand may present as pathologic fracture in a young adult. Enchondromas involving long bones are usually asymptomatic and are commonly an incidental finding identified on a radiograph obtained to evaluate the chest or an adjacent joint. Regional pain about an enchondroma is more frequently related to a nearby joint or a local soft-tissue disorder than to the tumor itself and may be the cause for incidental discovery of an asymptomatic enchondroma.

A common scenario is a patient with shoulder pain in whom there is a completely intramedullary cartilaginous lesion in the proximal humerus, which could represent an enchondroma or a low-grade chondrosarcoma. A thorough history and physical examination are necessary to evaluate the shoulder for other causes of the pain. Subacromial or acromioclavicular injection of a local anesthetic agent can help identify the origin of the pain. If

Table 1
Characteristics of Cartilage Tumors and Treatment Recommendations

Tumor Type	Pain	Adaptive or Aggressive Radiologic Changes*	Bone Scan	Histology	Treatment
Enchondroma	–	–	–	Enchondroma	Observation
Atypical enchondroma† (chondrosarcoma in situ)	+	–	+/–	Enchondroma	Observation or intralesional excision
Chondrosarcoma in situ	+/–	–	+/–	Grade I chondrosarcoma	Observation, intralesional excision, or (occasionally) wide excision
Low-grade chondrosarcoma	+	+	+	Grade I chondrosarcoma	Wide excision
Intermediate-grade chondrosarcoma	+	+	+	Grade II chondrosarcoma	Wide excision
High-grade chondrosarcoma	+	+	+	Grade III chondrosarcoma	Wide excision
Dedifferentiated chondrosarcoma	+	+	+	Dedifferentiated chondrosarcoma	Wide excision

* Adaptive radiologic changes include cortical thickening and expansion. Aggressive changes include cortical disruption and the presence of a soft-tissue mass.
† Synonymous with grade 0.5 chondrosarcoma, low-grade I chondrosarcoma, or borderline chondrosarcoma.

the pain resolves, it was likely secondary to an inflammatory syndrome in the shoulder, rather than being due to the proximal humerus lesion. The shoulder disorder should be treated appropriately, and the lesion, which is likely an enchondroma, should be periodically monitored for the development of clinical or radiographic signs or symptoms of tumor progression. If the pain persists despite appropriate treatment of the presumed shoulder disorder, the symptoms may be from the lesion, which can be either an enchondroma or a low-grade chondrosarcoma, necessitating further evaluation to differentiate between them.

Most patients with chondrosarcoma have pain.[9,10,12,14] In a study of 58 patients with intramedullary low-grade chondrosarcoma, Marco et al[14] found that 60% (35) had rest or night pain, 21% had vague regional pain, and 19% had lesions that were detected incidentally. Nearly 80% of patients with intermediate- or high-grade chondrosarcoma have pain.[6] Pathologic fractures occur in 3% to 8% of patients with chondrosarcoma.[6,9,14]

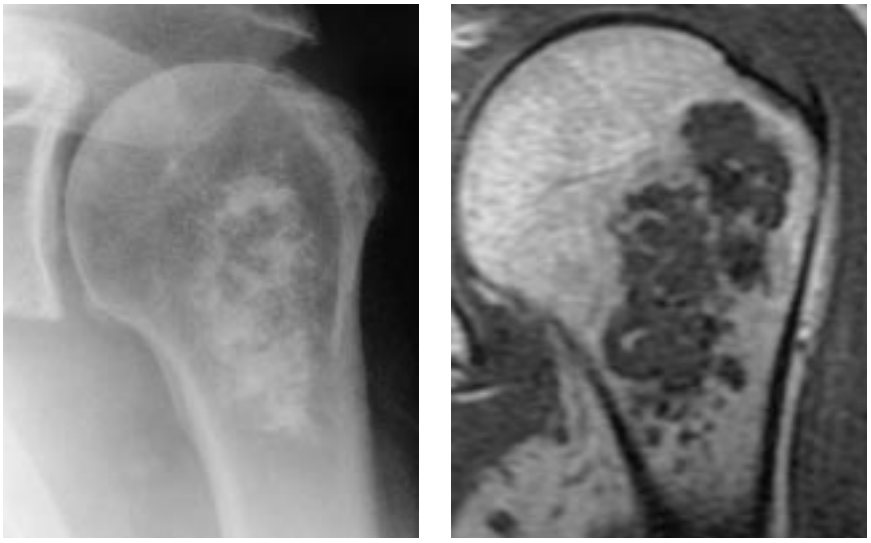

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Figure 1 **A,** Anteroposterior radiograph of the left proximal humerus and shoulder of an 82-year-old man without any pain. Note the calcified lesion without evidence of cortical erosion. **B,** T1-weighted (repetition time, 350 msec; echo time, 12 msec [350/12]) MR image of the left humerus shows tumor lobules present, with multiple satellites. The tumor did not destroy bone and was consistent with an enchondroma. Follow-up plain radiographs showed no evidence of progression.

Radiologic Findings

Enchondromas (Fig. 1) and low-grade intramedullary chondrosarcomas (Fig. 2) of long bones can have similar radiologic appearances. Both types of tumors demonstrate stippled calcifications, and both may display endosteal scalloping on plain radiographs.[1,15] They are commonly located in the metaphysis of the humerus, femur, or tibia. Calcification is manifested by punctate mineralization or popcornlike calcification. The margins of the tumor should be examined for osteolysis and endosteal scalloping. The extent and degree of endosteal scalloping correlate with the likelihood of the lesion being a chondrosarcoma.[10] In one study, Murphey et al[10] found that 71 (75%) of 95 patients with chondrosarcoma had endosteal scalloping of more than two thirds of the cortical thickness, compared with 8 (9%) of 92 patients with enchondroma.

Chondrosarcoma can demonstrate adaptive and aggressive radiologic signs. Cortical expansion and thickening are adaptive changes, and cortical disruption and soft-tissue masses are aggressive changes associated with chondrosarcoma.[1,10] Rosenthal et al[15] summarized the plain-radiographic and computed tomographic (CT) findings in low- and high-grade chondrosarcoma. Low-grade features include (1) dense calcifications forming rings or spicules, (2) widespread or uniformly distributed calcifications, and (3) eccentric lobular growth of a soft-tissue mass. High-grade features include (1) faint amorphous calcification, (2) large noncalcified areas, and (3) concentric growth of a soft-tissue mass. Lysis within a previously calcified area may be a sign of tumor progression. The primary exception to these radiologic findings is enchondroma in a short tubular bone of the hand, which frequently demonstrates marked endosteal scalloping, large areas of lysis, and cortical expansion.

A technetium-99m diphosphonate whole-body bone scan can provide some useful information about an intramedullary cartilaginous lesion. A whole-body bone scan with a high degree of radionuclide uptake within the lesion compared with an internal standard, such as the anterior superior iliac spine or acromioclavicular joint, is more consistent with chondrosarcoma than enchondroma.[10] Murphey et al[10] graded radionuclide uptake from grade 1 to grade 3, with grade 1 indicating uptake less than that in the anterior iliac crest; grade 2, uptake similar to that in the anterior iliac crest; and grade 3, uptake greater than that in the anterior iliac

crest. In their study of 51 patients with chondrosarcoma, 42 (82%) had grade 3 uptake, compared with 14 of 67 patients (21%) with enchondroma. However, most enchondromas demonstrate some activity on bone scan; therefore, that finding alone is not particularly worrisome. The bone scan can also help identify polyostotic disease.

Axial imaging with CT or magnetic resonance (MR) imaging can be helpful in evaluating the depth of endosteal scalloping and the size of the lesion and its soft-tissue component. Computed tomography is the study of choice to evaluate the osseous architecture for endosteal scalloping and bone disruption. Magnetic resonance imaging is particularly useful in determining the nonmineralized intramedullary extent of the tumor and soft-tissue extension. The axial and coronal images accurately demonstrate marrow replacement by tumor, providing measurements that can guide the surgeon when either an intralesional or a wide excision is performed. The relationship of a soft-tissue mass to important paraosseous structures, such as the joint capsule and the neurovascular bundle, is accurately demonstrated on MR images. The percentage of medullary fill of the lesion visualized on MR imaging is also useful information. Medullary fill greater than 90% is predictive of chondrosarcoma.[11] Noncontiguous foci of cartilage, or satellites (Fig. 1, B), are predictive of enchondroma if the medullary fill is less than 90%. Finally, a chest radiograph and usually a CT scan of the chest are obtained for staging.

Biopsy

The biopsy of a chondrosarcoma can be performed with closed or open techniques. Closed biopsy techniques with fine (20- to 23-gauge) or core needles are commonly utilized to confirm the diagnosis of a cartilaginous tumor that is clinically and radiographically a chondrosarcoma. A fine-needle biopsy directed by fluoroscopy or CT can be utilized if there is a soft-tissue component. Imaging may not be required if the soft-tissue mass is palpable. This procedure primarily yields material for cytologic and, to a lesser extent, histologic examination. If the tumor is located within bone, a core needle penetrates the bone more readily than a fine needle. A core-needle biopsy provides a cylinder of tissue, which can be examined both cytologically and histologically. Biopsy specimens should be taken from the areas of most concern, such as areas of bone destruction and those demonstrating a high degree of endosteal scalloping and lysis.

Experienced musculoskeletal pathologists can usually diagnose a high-grade chondrosarcoma if malignant cartilaginous cells are noted. A major drawback of needle-biopsy techniques, however, is sampling error due to tumor heterogeneity.[16,17] A high-grade cartilaginous tumor often contains low-grade or benign hyaline cartilage material.

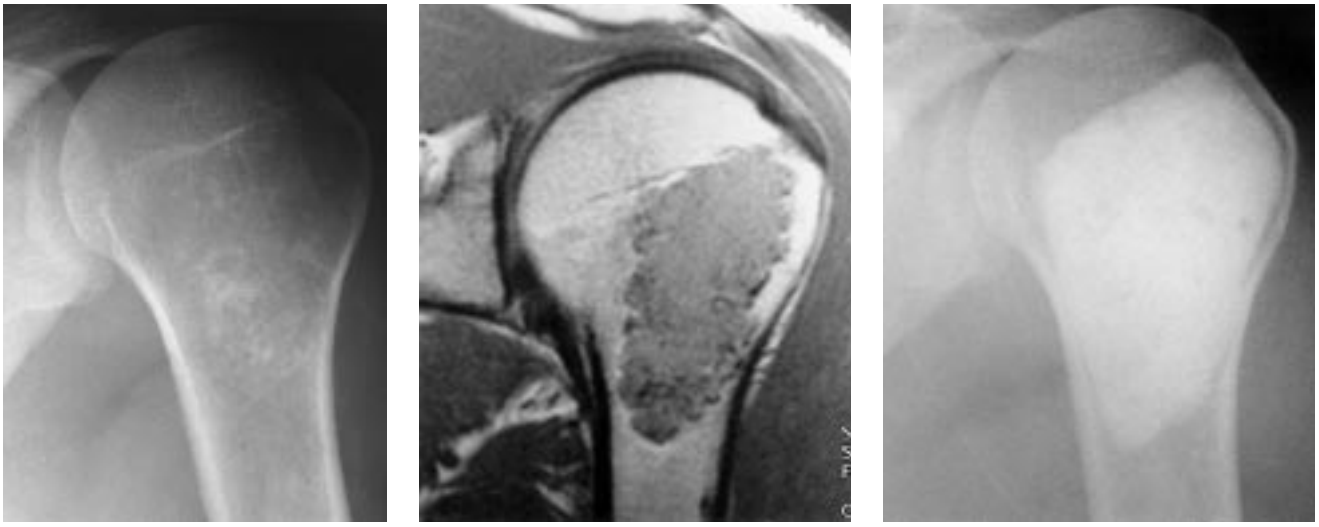

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Figure 2 **A,** Anteroposterior radiograph of the left proximal humerus of a 43-year-old man with progressively increasing shoulder pain, which was present at rest. Note the calcification with minimal endosteal scalloping. **B,** T2-weighted (3,500/16) MR image of the lesion in the proximal humerus. Biopsy revealed a low-grade chondrosarcoma. **C,** The patient was treated with intralesional excision, cauterization with phenol, and insertion of methylmethacrylate. The pain resolved completely.

The final pathologic study could conceivably reveal a chondrosarcoma despite a needle-biopsy diagnosis of enchondroma. Differentiating an enchondroma from a low-grade chondrosarcoma is often difficult, if not impossible, with the small amount of material obtainable by needle biopsy.

An open biopsy usually provides adequate tissue for diagnosis but is associated with surgical-site contamination and other complications associated with open procedures and general anesthesia. Confirmation of the viability of the tumor and the adequacy of the tissue sample should be obtained by frozen-section diagnosis at the time of the procedure.

Symptomatic intramedullary cartilaginous tumors that display neither adaptive radiologic changes (cortical thickening or expansion) nor aggressive radiologic changes (cortical disruption or soft-tissue mass) are likely to be enchondromas or low-grade chondrosarcomas. If the clinical presentation warrants further evaluation, a biopsy is recommended before definitive treatment. If an intermediate- or a high-grade cartilage tumor is identified on the basis of frozen-section analysis, the procedure should be terminated, and treatment deferred until a final pathology report is made. If the frozen section is consistent with an enchondroma or a low-grade chondrosarcoma, some surgeons would proceed with intralesional excision with or without adjuvant therapy.

Performing a simultaneous intralesional excision can obviate a second operative procedure, provide curative treatment, and minimize bleeding with subsequent seeding of tumor cells within the incision.[15] However, the patient must be counseled preoperatively that the tumor grade (and thus the optimal treatment) may change with the final diagnosis on permanent sections. Definitive treatment should be based on the highest grade of tumor present. If the diagnosis is an enchondroma or a low-grade chondrosarcoma, close observation is appropriate. If intermediate- or high-grade chondrosarcoma is identified within any portion of the tumor, a secondary wide excision may be required. To minimize local contamination of the tissues by chondrosarcoma cells, it is important to protect the surrounding tissues during the curettage and achieve meticulous hemostasis after intralesional treatment. If the biopsy and intralesional excision are performed properly, the definitive oncologic procedure and outcome should not be adversely affected if more aggressive surgical intervention is required.

Although simultaneously performing a biopsy and an intralesional excision for an intramedullary cartilaginous tumor has advantages, most surgeons prefer to wait for the final pathologic diagnosis before further treatment. An intralesional or wide excision with removal of the entire biopsy track and previously exposed tissue is then performed. However, the pathologist may identify higher-grade tumor in the specimen removed at the definitive excision than was originally found at biopsy. Delaying the definitive treatment while waiting for a final biopsy diagnosis does not completely avoid the possibility that a change in the preoperative diagnosis may occur once the entire specimen is examined.

Some authors have advocated not obtaining biopsy specimens of cartilaginous tumors that are clinically and radiographically chondrosarcomas, although this is not a widely held opinion.[18] These chondrosarcomas are painful and may have an associated soft-tissue mass. A high degree of endosteal scalloping and adaptive and aggressive radiologic findings are seen. Although these tumors can be low-grade chondrosarcomas, they are more often intermediate- or high-grade chondrosarcomas. Chondrosarcomas demonstrating these clinical and radiographic signs should be treated with wide excision. Some tumor surgeons would proceed with a wide excision without performing a biopsy, thereby avoiding the inevitable contamination of the biopsy site with tumor cells. The specimen is then sent for final gross and histologic diagnosis. However, although this procedure is theoretically better, only a very experienced tumor surgeon should make these decisions.

Clinicopathologic Grading

Chondrosarcomas are graded on the basis of the cytologic and histologic appearance[8,12,13,15,19] (Fig. 3), combined with the clinical and radiologic presentation. Most authors grade chondrosarcomas from grade I to grade III.[8,12,13,15,19] The diagnosis of grade II (intermediate-grade) and grade III (high-grade) chondrosarcoma can usually be made on the basis of either cytologic or histologic features.[12,13] Grade I (low-grade) chondrosarcoma, however, has cytologic features similar to those of enchondroma. Therefore, histologic criteria must be combined with clinical and radiologic findings to differentiate enchondroma (Fig. 4) from low-grade chondrosarcoma.[12,13]

Histologically, both enchondromas and low-grade chondrosarcomas are composed of hyaline cartilage cells. A low-grade chondrosarcoma should be suspected if there are (1) many cells with plump nuclei, (2) more than an occasional binucleate cell, and (3) giant cartilage cells with large nuclei or with clumps of chromatin.[19] Further differentiation between an enchondroma and a low-grade chondrosarcoma is then

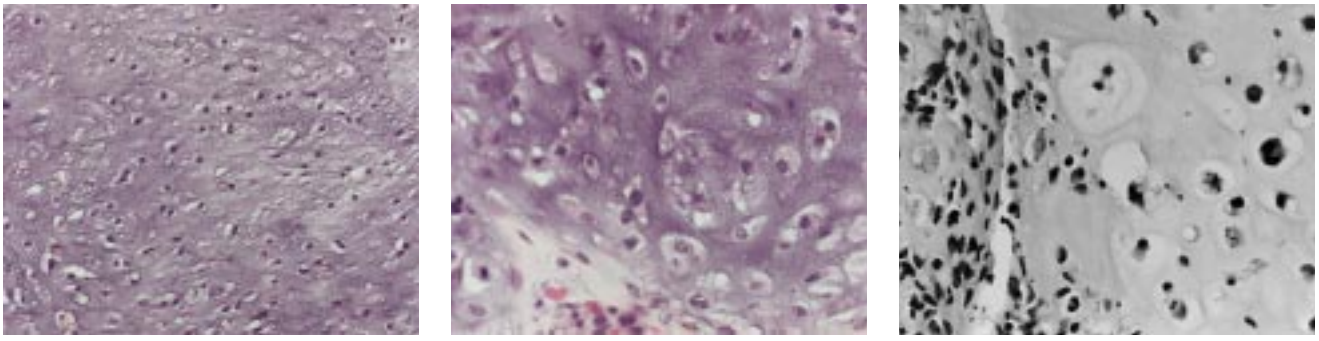

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Figure 3 **A,** Low-grade chondrosarcoma (hematoxylin-eosin, original magnification ×100). This tumor is well-differentiated. Hypercellularity is noted, but the cartilage matrix may be easily identified. There are numerous binucleate cells within lacunae and few atypical cells. **B,** Higher-magnification view of the same tumor (hematoxylin-eosin, original magnification ×250). Mild pleomorphism and hyperchromatism are apparent, and binucleate cells are seen. The tumor had a well-differentiated cartilage matrix. **C,** Intermediate-grade chondrosarcoma (hematoxylin-eosin, original magnification ×250). The tumor displays distinct pleomorphism, with some very large hyperchromatic cells.

possible by examining the tissue pattern of the cartilage cells and the lamellar bone, as described by Mirra et al.[12] The enchondroma pattern consists of nodules of hyaline cartilage that are encased by lamellar bone. These nodules are separated from each other by normal marrow. The low-grade chondrosarcoma pattern consists of cartilage cells that permeate marrow spaces and completely replace the marrow fat. The cartilage cells directly abut and surround the lamellar bone in the chondrosarcoma pattern. Other histologic findings of chondrosarcoma include (1) malignant bands of fibrosis, (2) chondrosarcomatous invasion of marrow fat, (3) malignant invasion of the haversian system, and (4) a soft-tissue mass.

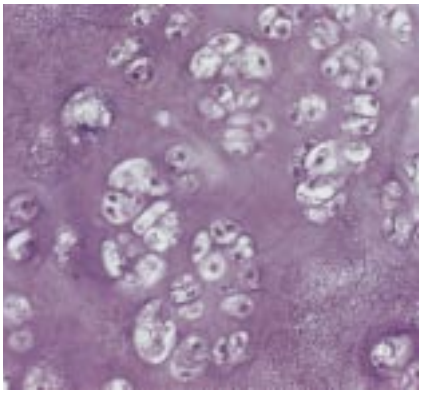

Figure 4 Enchondroma (hematoxylin-eosin, original magnification ×100). Note the hypocellularity of the lesion and the uniformity in size and staining features of the cells. The hyaline cartilage matrix is readily apparent.

Occasionally, a painful cartilaginous lesion in a long bone has the radiologic appearance of a low-grade chondrosarcoma (e.g., lytic areas or high-grade endosteal scalloping without adaptive or aggressive radiographic changes) and the histologic appearance of an enchondroma. This lesion is referred to as a grade 0.5 chondrosarcoma by some authors; others may describe it as a borderline chondrosarcoma, low grade 1 chondrosarcoma, grade 0 chondrosarcoma, painful enchondroma, or atypical enchondroma. We prefer the term "chondrosarcoma in situ," which implies that the lesion is benign and should not metastasize unless there is malignant transformation. We also believe that tumors with both the radiologic and the histologic appearance of a low-grade chondrosarcoma should be considered chondrosarcomas in situ because these lesions do not metastasize if treated properly.[4,14,20,21]

Cartilaginous lesions in the hand and pelvis behave differently than intramedullary cartilaginous lesions of the long bones with similar histologic appearances.[1] Enchondromas of the short tubular bones in the hand frequently have multinucleated cells, as well as increased cellularity that resembles the appearance of grade 1 chondrosarcoma. Although these tumors occasionally recur after intralesional treatment, they do not metastasize. However, most patients with a histologically similar lesion in the pelvis will have a local recurrence after intralesional excision.[21-23]

Staging

Chondrosarcomas are staged according to the system described by Enneking.[24] Nonmetastatic low-grade chondrosarcomas are considered stage I neoplasms. Nonmetastatic intermediate- and high-grade chondrosarcomas are stage II. Metastatic chondrosarcomas are stage

III. Tumors are then subclassified as either stage A or stage B on the basis of whether they are located within the bone or extend outside the bone. For example, a low-grade intramedullary chondrosarcoma without metastases is stage IA, whereas a high-grade nonmetastatic chondrosarcoma with an associated soft-tissue mass is stage IIB.

Enchondromas may be staged by using the Enneking staging system for benign tumors.[24] In that system, a stage 1 tumor is latent (i.e., a tumor that does not progress or that heals spontaneously). A stage 2 tumor is active (i.e., it progresses but respects natural barriers, such as the bone cortex). A stage 3 tumor is aggressive (i.e., it progresses and will ultimately destroy natural barriers). Enchondromas are usually stage 1 but are occasionally stage 2.

Types of Surgical Excisions

Enneking[24] defined surgical margins for bone tumors. An intralesional excision is a procedure that enters the tumor during removal. Intralesional excisions may be planned or inadvertent (i.e., those that occur during attempted wide excision). A planned intralesional excision grossly debulks the tumor through a large cortical window, which conceivably leaves microscopic and macroscopic tumor in the tumor bed. Intralesional margins can be extended by use of an adjuvant, such as phenol or liquid nitrogen. A marginal excision passes through the reactive zone around the tumor, which probably contains microscopic satellite lesions of the tumor. These microscopic deposits remain in the excision bed. A wide margin includes a cuff of normal tissue completely encircling the tumor. Wide excisions remove the reactive zone with its microscopic satellites. The margin definitions are the same for limb salvage and amputation.

Treatment of Enchondromas

Enchondroma is a benign latent lesion or, at worst, an active lesion that does not metastasize and rarely undergoes malignant degeneration. Enchondromas can be treated nonoperatively unless they are symptomatic or enlarging or unless there is an impending or existing fracture. Most patients with an enchondroma are asymptomatic and are best followed up by sequential clinical assessments and radiographic evaluations (i.e., a set of orthogonal plain radiographs) in 3 months. If there is no clinical or radiographic change at that time, another set of radiographs is obtained 6 months later. In the absence of progressive changes (e.g., increased endosteal scalloping or osteolysis), obtaining repeat clinical and radiographic examinations once a year is reasonable. Patients are told to return for examination if symptoms develop. Bone scanning, CT, and MR imaging are usually not necessary for the evaluation of well-calcified lesions. Extensive noncalcified or lytic areas should be followed with serial MR imaging studies.

A few patients with enchondromas present with vague regional pain about the involved bone. The pain is usually related to joint or soft-tissue pathologic changes. Nonoperative measures, such as physical therapy and differential injections, can be used. If the pain persists or worsens despite nonoperative treatment or if there is radiographic evidence of tumor progression, the pain may be originating from the lesion.

The most worrisome symptoms are rest pain and night pain (often termed "nonmechanical pain"), which are considered an ominous sign suggesting the presence of a malignant neoplasm. Patients with these symptoms or lesional progression should undergo further evaluation with axial imaging and a biopsy.

Enchondromas involving the short tubular bones of the hand usually present as pathologic fractures. If a fracture is present, the digit is immobilized until union occurs. If the lesion is large and another pathologic fracture is expected, an intralesional excision and reconstruction with autogenous or allograft bone can be performed. Local recurrence is unusual. Some surgeons prefer to treat the fracture and the tumor at the time of presentation. Occasionally, internal fixation is required to help stabilize the fracture. Adjuvant therapy may help decrease local recurrence rates but is not routinely utilized.

Treatment of Chondrosarcomas in Situ

The treatment of low-grade chondrosarcomas without adaptive or aggressive radiologic changes is controversial. Most authors recommend a wide excision for treatment of low-grade chondrosarcoma. In three studies,[6,7,22] wide excisions were associated with lower local recurrence rates compared with intralesional excisions. However, the authors of those studies combined low-grade and high-grade chondrosarcomas, as well as axial and appendicular chondrosarcomas, in their analyses of the surgical margin.

There is a subset of patients with low-grade chondrosarcomas that can be treated with intralesional excision with adjuvant therapy without compromise of the oncologic outcome.[4,14,20,21] Adjacent bone and joint preservation and improved function are the major advantages of an intralesional excision compared with a wide excision, which usually requires bone and joint sacrifice. These patients have intramedullary low-grade chondrosarcoma (stage IA) of the appendicular skeleton, which can demonstrate a high degree of endosteal scalloping

but not adaptive or aggressive radiologic signs (Fig. 2). These tumors are usually painful. They are histologically low-grade chondrosarcomas and do not metastasize when treated properly. Thus, they are more appropriately described as chondrosarcomas in situ.

In a large retrospective review of the data on 58 patients with intramedullary low-grade chondrosarcoma of a long bone treated with intralesional excision with or without adjuvant therapy, Marco et al[14] demonstrated low local recurrence rates. There were no local recurrences or metastases in the 57 patients who met criteria for the diagnosis of chondrosarcoma in situ after a minimum follow-up interval of 5 years. The only local recurrence developed in a patient with cortical disruption, thickening, and expansion, as well as a soft-tissue mass. By definition, this patient did not have a chondrosarcoma in situ. The joint was preserved in 92% of the patients when it was in jeopardy.

Bauer et al[20] reported on 22 patients with intramedullary low-grade chondrosarcoma (chondrosarcoma in situ) of a long bone treated by an intralesional excision. One patient had a local recurrence, and there were no metastases.

Schreuder et al[4] treated 9 patients with intramedullary low-grade chondrosarcoma (chondrosarcoma in situ) with intralesional excision plus adjuvant liquid nitrogen. They had no local recurrences at a mean follow-up interval of 26 months.

Marcove et al[21] reported on intralesional excision plus cryosurgery for low- and medium-grade chondrosarcoma. There were no local recurrences in the four patients who met criteria for the diagnosis of chondrosarcoma in situ of a long bone. Recurrences were seen in three of nine patients with grade II chondrosarcoma of a long bone or a grade I or grade II tumor of the axial skeleton.

The combined local recurrence rate in these studies was 1% (1 of 92 patients) for patients with tumors that met the criteria for diagnosis of chondrosarcoma in situ. None of these patients had metastases or died of disease.

It should be noted that chondrosarcoma in situ can demonstrate malignant behavior. Lee et al[5] noted that 2 of 16 patients with atypical enchondroma had metastases, and 1 patient died of the disease. Chondrosarcoma in situ is thus an appropriate designation for a symptomatic intramedullary cartilaginous tumor without adaptive or aggressive radiologic changes but with histologic findings consistent with an enchondroma or a low-grade chondrosarcoma. The term implies that the tumor is a premalignant lesion that will not metastasize if properly treated. Appropriate intervention and follow-up are justified, yet the patient is not given the diagnosis of a malignant condition.

Technique for Intralesional Excision

Intralesional excisions may be used in carefully selected individuals. The exposure is limited initially until the biopsy has been performed. Sponges are used to protect the exposed muscle and soft tissues from contamination with tumor cells. A high-speed burr is used to open the humerus. Alternatively, a trephine can be used to procure a sample that preserves the interface between the tumor and the cortical endosteum. Care should be taken to minimize spillage. Biopsy specimens are obtained from the most worrisome areas with a curette. A frozen section is also obtained. The surgeon should discuss the case with the pathologist before the biopsy to factor in the clinical and radiologic features. If the frozen-section findings are consistent with an intermediate- or high-grade chondrosarcoma, the defect is filled with bone wax or methylmethacrylate to prevent tumor spillage, and the wound is closed after meticulous hemostasis has been established. After the final pathologic diagnosis, the definitive procedure is performed. If the frozen section is consistent with an enchondroma or a low-grade chondrosarcoma, the surgeon can stop and wait for the final pathologic diagnosis or proceed with an intralesional excision.

The intralesional excision requires a slightly more extensile exposure than the biopsy. Sponge protection is augmented to cover all exposed muscle and soft tissue, which helps prevent implantation of sarcoma cells. Avoiding unnecessary dissection and exposure is critical so that a salvage procedure can be performed if the final diagnosis warrants a wide excision. A burr is used to unroof the tumor cavity. Another technique is to connect multiple drill holes with an osteotome. A Kerrison rongeur is effective in enlarging the hole until there is complete visualization of the entire cavity. The lesion is excised with progressively smaller instruments until all gross tumor has been removed. Internal burring is then performed throughout the cavity, thereby extending the margins by another millimeter. A fiberoptic light is used for direct visualization of the entire tumor cavity.

Adjuvant Therapy

Most authors believe that adjuvant therapy is required to kill remaining microscopic foci of tumor.[3,4,14,21] Some prefer to cauterize the cavity with both electrocautery and phenol. A phenol and glycerol solution is dabbed on the bone with a cotton-tipped applicator. Phenol percentages as high as 80% are used. The phenol is removed by lavaging the cavity with absolute alcohol. Further lavage with a high-pressure pulsatile system is then performed.

An alternative to phenol cauterization is cryosurgery.[21] Cryosurgery effectively extends the margin of resection beyond that achieved by mechanical curettage and burring. This method kills tumor cells by mechanically disrupting the cell membrane with intracellular ice crystals and poisoning them by creating intracellular electrolyte imbalances. Cryosurgery also causes capillary scarring, which necroses both tumor cells and host bone. It is most effective when the lesion is frozen rapidly and thawed slowly. One treatment consists of three cycles in succession. The depth of freeze is governed by the size of the defect, the volume of liquid nitrogen delivered, the effectiveness of local heat-exchange mechanisms (e.g., blood flow) in dissipating the cold, and the duration of the freeze. Some surgeons monitor the depth of the freeze with multiple temperature probes around the lesion. Freezing can usually be assessed on the basis of the amount of frost or the size of the ice ball created.

For selected stage IA chondrosarcomas (chondrosarcomas in situ), successful local control is obtained after freezing the bone until the periosteum starts to frost.[14,21] The general technique is as follows: Hemostasis is obtained by using a tourniquet when possible; alternatively, electrocautery, argon-beam laser, or a thin layer of bone wax may be used. The bone cavity should be kept horizontal to avoid spillage of the liquid nitrogen. The soft tissues are retracted widely so that the skin is not inadvertently frozen. Liquid nitrogen is instilled rapidly by pouring it in the cavity or by using a spray gun. The liquid is then allowed to evaporate. The bone window must not be occluded, because nitrogen embolization can occur when trapped nitrogen expands during its conversion from liquid to gas. Ice or frozen blood bubbles are broken up to release captured nitrogen. The bone is thawed slowly, and the process is then repeated twice. In selected cases, two cycles may be sufficient.[25]

The remaining shell of bone contains some necrotic bone, which is left in place as autogenous graft. The cortical defect weakens the bone. The use of adjuvant cryotherapy may cause increased fracture rates during the revascularization phase of bone healing compared with untreated intralesional defects.

Protection of the bone during the remodeling and revascularization phase is recommended to decrease the risk of pathologic fractures. Defect reconstruction and activity modification help protect the bone. Partial weight bearing with crutches is utilized to protect lower-extremity bone defects. Avoidance of twisting of both upper and lower extremities is also recommended. Most sporting activities are prohibited for 2 years to allow remodeling and revascularization. Although most patients feel that they can resume normal activity, they must be reminded that the bone will be weak for as long as 2 years after the procedure.

Reconstruction After Intralesional Excision

Although an intralesional excision usually preserves the adjacent joint and most of the bone cylinder, reconstruction is required to prevent fractures through the weakened bone. Methylmethacrylate reconstruction provides immediate stability, avoids the morbidity of autogenous bone graft, facilitates the postoperative radiologic evaluation for signs of recurrence, and may kill residual microscopic tumor cells with thermotherapy. The cement is molded into the cavity, creating a smooth cortical margin. If the osseous defect is large, internal fixation with threaded pins embedded into the cement can be added. Alternative reconstructions include autogenous or allogeneic bone graft or bone-graft substitutes (Fig. 5). Plate-and-screw fixation may be used to reinforce this reconstruction. Although long intramedullary devices may decrease the risk of fracture, this type of fixation may spread tumor cells within the bone and adjacent soft tissue. The wound is closed in the usual manner over closed suction.

Gentle, early range-of-motion exercises of the joint are encouraged. The fracture rate ranges from 10% to 20% after intralesional excision.[14,25] Patients should therefore modify their activity until the bone strength is restored, which may require up to 2 years of bone remodeling.

Final Diagnosis and Follow-up

The final diagnosis and tumor grade are determined after the pathologist has evaluated the entire specimen. Proper treatment is dictated by the highest grade of tumor present in the excised tissue. If a diagnosis of chondrosarcoma in situ is rendered, careful follow-up with clinical and radiologic examinations is recommended to monitor for local recurrence or distant metastases. If an intermediate- or high-grade tumor is seen, wide excision is recommended. If the intralesional excision was done properly, so as to minimize tumor contamination, a wide excision with limb preservation can then be performed.

Treatment of Chondrosarcomas With Adaptive or Aggressive Radiologic Changes

Several studies have demonstrated that adequate surgical margins lower the risk of local recurrence in patients with chondrosarcoma.[5,7-9,23] Gitelis et al[7] reported a 6% local recurrence rate if adequate margins were achieved, compared with a 69% local recurrence rate in patients with inadequate surgical margins. Although an intralesional excision

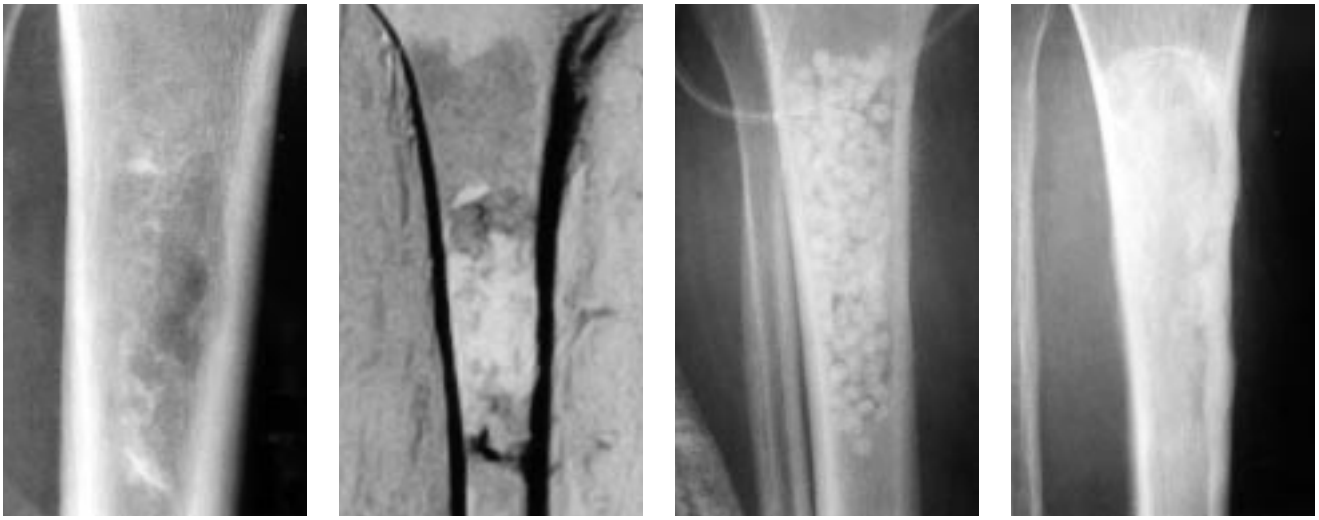

Figure 5 **A,** Lateral radiograph of the right proximal tibia of a 43-year-old woman with leg pain shows a calcified lesion in the tibial diaphysis, as well as mild endosteal erosion associated with the tumor. **B,** T2-weighted (1,900/80) MR image demonstrates mild endosteal erosion and the full extent of the tumor. **C,** Postoperative radiograph after biopsy and excision of a low-grade chondrosarcoma (grade I, stage IA). The bone was cauterized with phenol and filled with a bone-graft substitute (calcium sulfate). **D,** Radiograph obtained 2 years postoperatively shows bone repair with dense ossification. The patient's pain had resolved.

with adjuvant therapy provides adequate margins in patients with chondrosarcoma in situ, this method does not provide adequate margins in most patients with higher grades of chondrosarcoma. A wide excsion is thus recommended for intermediate- and high-grade chondrosarcomas of long bones.

Marcove et al[21] reported a 33% local recurrence rate in nine patients with intermediate-grade chondrosarcoma in a long bone treated with intralesional excision plus cryosurgery. Metastases developed in one of these patients, and only one remained disease-free after a subsequent wide excision. Wide margins are probably required to obtain adequate local control even in the case of low-grade chondrosarcomas in long bones with adaptive or aggressive radiologic findings (Fig. 6).

Marco et al[14] reported that one patient with a low-grade chondrosarcoma with cortical expansion, thickening, and disruption, as well as a soft-tissue mass, had a local recurrence after an intralesional excision combined with cryosurgery. The local recurrence was a dedifferentiated chondrosarcoma.

Wide excisions of chondrosarcomas involving the axial skeleton are associated with lower local recurrence rates (13% to 25%)[26,27] compared with intralesional procedures (67% to 100%).[21-23] Tsuchiya et al[22] treated two patients with borderline chondrosarcoma (chondrosarcoma in situ) of the pubis. One patient underwent an intralesional

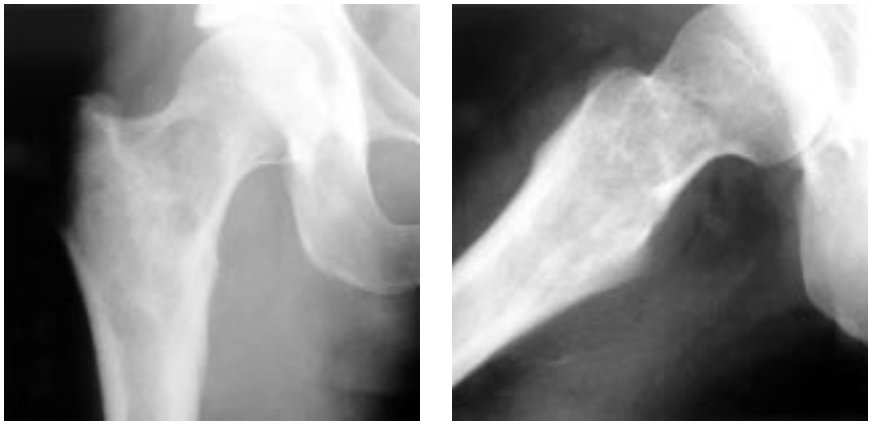

Figure 6 Anteroposterior **(A)** and lateral **(B)** radiographs of the right proximal femur of a 41-year-old man with a painful right hip show adaptive changes of cortical thickening and expansion. The grade I chondrosarcoma was treated by wide resection.

excision without adjuvant therapy, and one patient underwent a marginal excision. Recurrent disease developed in both patients, and one patient died of the disease.

Ozaki et al[26] had a 67% local recurrence rate in nine patients with low-grade chondrosarcomas of the pelvis and sacrum that had been contaminated intraoperatively during an attempted wide excision. Soft-tissue extension was noted in eight of these patients.

Marcove et al[21] treated two patients with intermediate-grade chondrosarcoma of the sacrum and pelvis with intralesional excisions combined with cryosurgery. Both patients had local recurrences.

Wide excisions are also recommended for chondrosarcomas involving the ribs, the proximal fibula, or the distal clavicle, because resection of these bones can be accomplished without significant morbidity.

Wide excisions create intercalary or articular defects. This type of procedure requires major reconstruction (Fig. 7). The options for intercalary reconstruction include allograft, autograft, vascularized autograft, and implant. The options for joint reconstruction include arthrodesis with autograft or allograft, arthroplasty with a modular oncology prosthesis, allograft prosthetic composite, and osteoarticular allograft.[26,28,29]

Major intercalary or joint reconstruction after a wide excision is associated with very significant morbidity and functional limitations. The reported complications include infection, allograft nonunion, allograft fracture, allograft dissolution, implant fracture, and implant loosening.[14] Most oncologic surgeons permanently restrict the function of their patients after major joint reconstruction. Patients are usually limited to low-impact stress to improve the durability of the replaced joint.

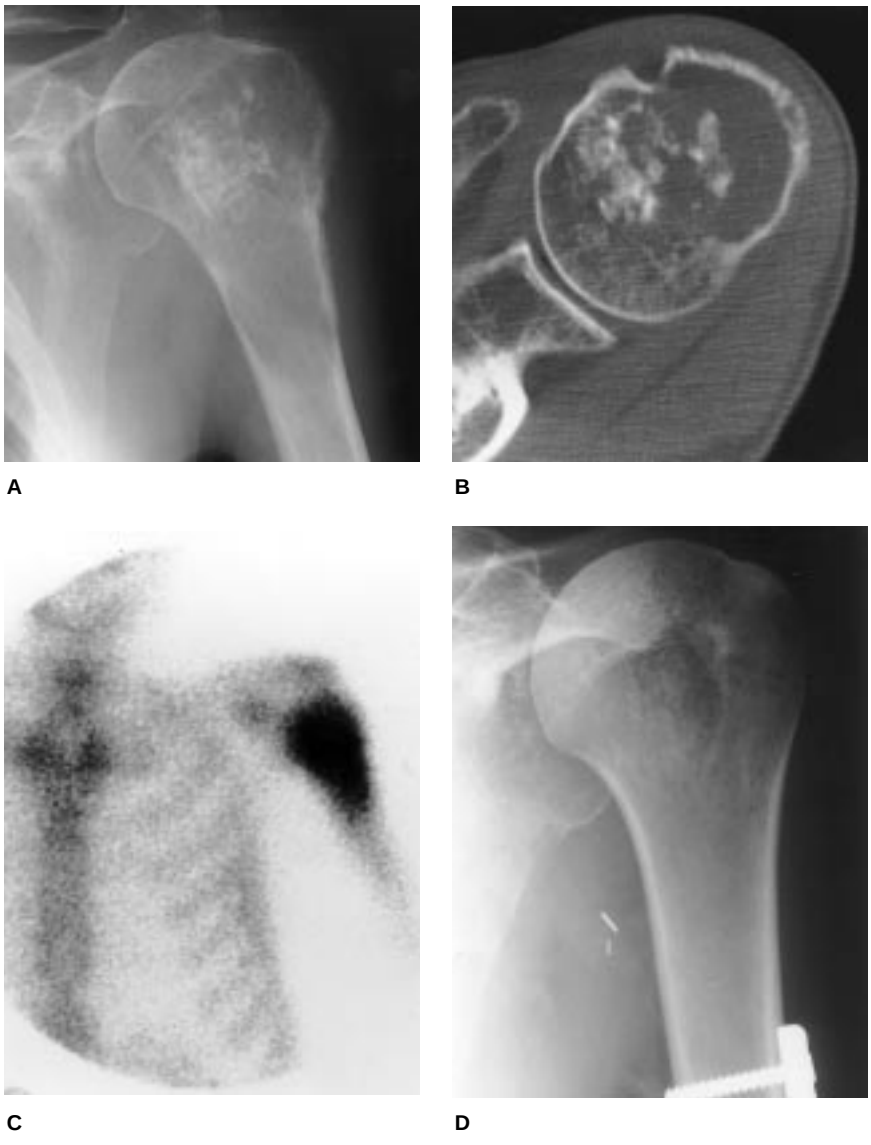

Figure 7 **A,** Anteroposterior radiograph of the left proximal humerus of a 74-year-old man with a painful shoulder. Note the calcified lesion involving the humeral metaphysis. There is marked endosteal scalloping and some bone destruction. **B,** CT scan of the humerus demonstrates a large area of lysis and cortical thinning. **C,** Technetium bone scan reveals intense uptake in the proximal humerus. **D,** Postoperative radiograph of the proximal humerus after wide excision of a low-grade (grade I) chondrosarcoma. There was cortical breakthrough by tumor (stage IB). The proximal humerus was replaced by an osteoarticular allograft.

Summary

The diagnosis and treatment of cartilaginous tumors is dependent on the clinical presentation, the location of the lesion, the radiologic findings, and the histologic grade of the tumor. Redefining the current diagnostic terminology should help determine the proper treatment for these tumors. The term enchondroma should be utilized to describe an asymptomatic intramedullary cartilaginous lesion. In the hand, an enchondroma can exhibit cortical expansion, lysis, and endosteal scalloping. Enchondroma

in a long bone can exhibit some endosteal scalloping but should not demonstrate lysis, cortical expansion, thickening, disruption, or associated soft-tissue masses. Histologically, enchondromas are composed of islands of hyaline cartilage encased by lamellar bone. Most are treated appropriately by periodic observation.

Chondrosarcoma in situ is a symptomatic, intramedullary cartilaginous tumor of a long bone without radiologic evidence of either adaptive changes (cortical expansion or thickening) or aggressive changes (cortical disruption or soft-tissue mass) and with the histologic features of an enchondroma or a low-grade chondrosarcoma (stage IA). Occasionally, a chondrosarcoma in situ is asymptomatic but has a high degree of endosteal scalloping or medullary fill.

Chondrosarcoma in situ is a premalignant lesion that warrants close observation with clinical and radiographic evaluation. Patients with persistent pain or progressive radiologic findings can be treated with intralesional excision combined with adjuvant therapy. This procedure preserves the joint and provides improved functional outcome potential compared with wide excision. Chondrosarcoma in situ does not metastasize or recur if treated properly. This designation is preferable to grade 0.5 chondrosarcoma, low grade 1 chondrosarcoma, or borderline chondrosarcoma because those terms imply that the patient has a malignant condition rather than a premalignant one. We also prefer the term chondrosarcoma in situ to the term atypical enchondroma because the latter implies benignity, which can downplay the necessity for treatment or long-term follow-up. Careful follow-up for 10 years is recommended to monitor for local recurrence.

A cartilaginous tumor of a long bone that is histologically a low-grade chondrosarcoma and exhibits a soft-tissue mass or cortical expansion, thickening, or disruption is designated a low-grade chondrosarcoma. Such tumors are commonly located in the long bones and pelvis. They rarely occur in the hand. Cytologically, low-grade chondrosarcomas resemble enchondromas. Histologically, however, they exhibit the criteria described by Mirra et al.[12] The most common finding is the chondrosarcomatous permeation pattern. A wide excision is recommended for these lesions.

Intermediate, high-grade, and dedifferentiated chondrosarcomas are more aggressive tumors. They are associated with higher local recurrence and mortality rates. These tumors are usually painful and demonstrate adaptive and aggressive radiologic changes. A soft-tissue mass is often seen. The cytologic and histologic features are readily distinguished from those of enchondroma and low-grade chondrosarcoma. A wide excision is recommended to minimize the risk of local recurrence. Limb salvage with reconstruction is possible in most cases.

Cartilaginous lesions in the pelvis and sacrum are worrisome. These tumors frequently recur after intralesional procedures even if the histologic appearance is benign or suggestive of a low-grade neoplasm. Therefore, wide excisions are recommended for nearly all cartilaginous tumors of the pelvis and sacrum.

The diagnosis and treatment of cartilaginous tumors can be complex. Ideally, treatment involves a multidisciplinary team composed of a musculoskeletal surgeon, a radiologist, and a pathologist.

References

1. Unni KK: *Dahlin's Bone Tumors: General Aspects and Data on 11,087 Cases*, 5th ed. Philadelphia: Lippincott-Raven, 1996.
2. Geirnaerdt MJ, Hermans J, Bloem JL, et al: Usefulness of radiography in differentiating enchondroma from central grade 1 chondrosarcoma. *AJR Am J Roentgenol* 1997;169:1097-1104.
3. Quint U, Pingsmann A: Surgical treatment of enchondroma in long tubular bones: Preservation of function versus extensive excision in the humerus. *Arch Orthop Trauma Surg* 1995;114:352-356.
4. Schreuder HWB, Pruszczynski M, Veth RPH, Lemmens JAM: Treatment of benign and low-grade malignant intramedullary chondroid tumours with curettage and cryosurgery. *Eur J Surg Oncol* 1998;24:120-126.
5. Lee FY, Mankin HJ, Fondren G, et al: Chondrosarcoma of bone: An assessment of outcome. *J Bone Joint Surg Am* 1999;81:326-338.
6. Pritchard DJ, Lunke RJ, Taylor WF, Dahlin DC, Medley BE: Chondrosarcoma: A clinicopathologic and statistical analysis. *Cancer* 1980;45:149-157.
7. Gitelis S, Bertoni F, Picci P, Campanacci M: Chondrosarcoma of bone: The experience at the Istituto Ortopedico Rizzoli. *J Bone Joint Surg Am* 1981;63:1248-1257.
8. Evans HL, Ayala AG, Romsdahl MM: Prognostic factors in chondrosarcoma of bone: A clinicopathologic analysis with emphasis on histologic grading. *Cancer* 1977;40:818-831.
9. Bjornsson J, McLeod RA, Unni KK, Ilstrup DM, Pritchard DJ: Primary chondrosarcoma of long bones and limb girdles. *Cancer* 1998;83:2105-2119.
10. Murphey MD, Andrews CL, Flemming DJ, Temple HT, Smith WS, Smirniotopoulos JG: From the archives of the AFIP: Primary tumors of the spine—Radiologic pathologic correlation. *Radiographics* 1996;16:1131-1158.
11. Colyer RA, Sallay P, Buckwalter K, Van Bastelaer F: MRI assessment of chondroid matrix tumours, in *Limb Salvage: Current Trends—Proceedings of the 7th International Symposium*. Singapore: International Symposium of Limb Salvage, 1993, pp 89-93.
12. Mirra JM, Gold R, Downs J, Eckardt JJ: A new histologic approach to the differentiation of enchondroma and

chondrosarcoma of the bones: A clinicopathologic analysis of 51 cases. *Clin Orthop* 1985;201:214-237.
13. Sanerkin NG: The diagnosis and grading of chondrosarcoma of bone: A combined cytologic and histologic approach. *Cancer* 1980;45:582-594.
14. Marco RAW, Lane J, Huvos A, Kawai A, Healey JH: Intralesional excision of intramedullary low grade chondrosarcoma of the extremity. Presented at the 67th Annual Meeting of the American Academy of Orthopaedic Surgeons, Orlando, Fla, March 15-19, 2000.
15. Rosenthal DI, Schiller AL, Mankin HJ: Chondrosarcoma: Correlation of radiological and histological grade. *Radiology* 1984;150:21-26.
16. Tunç M, Ekinci C: Chondrosarcoma diagnosed by fine needle aspiration cytology. *Acta Cytol* 1996;40:283-288.
17. Ayala AG, Ro JY, Fanning CV, Flores JP, Yasko AW: Core needle biopsy and fine-needle aspiration in the diagnosis of bone and soft-tissue lesions. *Hematol Oncol Clin North Am* 1995;9:633-651.
18. Barnes R, Catto M: Chondrosarcoma of bone. *J Bone Joint Surg Br* 1966;48:729-764.
19. Lichtenstein L, Jaffe HL: Chondrosarcoma of bone. *Am J Pathol* 1943;19:553-574.
20. Bauer HCF, Brosjö O, Kreicbergs A, Lindholm J: Low risk of recurrence of enchondroma and low-grade chondrosarcoma in extremities: 80 patients followed for 2-25 years. *Acta Orthop Scand* 1995;66:283-288.
21. Marcove RC, Stovell PB, Huvos AG, Bullough PG: The use of cryosurgery in the treatment of low and medium grade chondrosarcoma: A preliminary report. *Clin Orthop* 1977;122:147-156.
22. Tsuchiya H, Ueda Y, Morishita H, et al: Borderline chondrosarcoma of long and flat bones. *J Cancer Res Clin Oncol* 1993;119:363-368.
23. Ozaki T, Lindner N, Hillmann A, Rödl R, Blasius S, Winkelmann W: Influence of intralesional surgery on treatment outcome of chondrosarcoma. *Cancer* 1996;77:1292-1297.
24. Enneking WF: A system of staging musculoskeletal neoplasms. *Clin Orthop* 1986;204:9-24.
25. Aboulafia AJ, Rosenbaum DH, Sicard-Rosenbaum L, Jelinek JS, Malawer MM: Treatment of large subchondral tumors of the knee with cryosurgery and composite reconstruction. *Clin Orthop* 1994;307:189-199.
26. Ozaki T, Hillmann A, Lindner N, Blasius S, Winkelmann W: Chondrosarcoma of the pelvis. *Clin Orthop* 1997; 337:226-239.
27. Kawai A, Healey JH, Boland PJ, Lin PP, Huvos AG, Meyers PA: Prognostic factors for patients with sarcomas of the pelvic bones. *Cancer* 1998;82:851-859.
28. Eriksson AI, Schiller A, Mankin HJ: The management of chondrosarcoma of bone. *Clin Orthop* 1980;153:44-66.
29. van Loon CJM, Veth RPH, Pruszczynski M, Wobbes T, Lemmens JAM, van Horn J: Chondrosarcoma of bone: Oncologic and functional results. *J Surg Oncol* 1994;57:214-221.