CHAPTER 36

General Principles of Tumor Management

Tumors of the Musculoskeletal System

Tumors of the musculoskeletal system present a variety of challenges. Many benign tumors are easily managed by the pediatric orthopaedist with a good outcome, but occasionally serious complications develop. Patients with malignant tumors are best treated by surgeons with specific expertise in oncology. Inexperience may lead to fatal treatment errors even at the stage of primary biopsy. Modern survival rates exceed those of 20 years ago by manyfold, largely owing to the development of the field of orthopaedic oncology and the armamentarium of surgical and adjuvant therapies.

DIAGNOSIS

The presentation of a patient with a musculoskeletal tumor is often a useful clue to the diagnosis. A child who presents with a pathologic fracture without prior symptoms most often has a benign lesion of bone that has gradually weakened the cortex, resulting in a fatigue fracture through a cystic lesion. On the other hand, a gradually enlarging mass accompanied by increasing pain, especially at night, suggests a diagnosis of primary malignancy. Soft tissue tumors most often are painless and come to medical attention because the patient or parent notices a mass. The more aggressive the tumor, the shorter and more alarming is the period of onset.

The presence of a palpable mass is an important finding on physical examination. The examiner should determine its size, consistency, mobility, and whether it is painful on palpation. A rapidly growing lesion is more likely to be malignant than benign. In taking the history, it is helpful to compare the size of the mass to a dime, a nickel, a quarter, or a half-dollar, or, if the tumor is larger, to a tennis ball, a football, and so on. It is important to measure and record the size of the tumor as accurately as possible for comparison and subsequent examinations.

The consistency of the mass is determined next. Is it firm or soft? Does it feel cystic or bony and hard? A cystic or fluid-filled mass should be examined with a flashlight to determine whether it transilluminates. In general, fluid-filled masses are commonly benign, whereas large, hard masses are more likely to be malignant. Is there a distinct change from normal to abnormal at the margins of the mass? Is the mass of the same consistency as the surrounding normal tissue? Malignant swellings usually invade the adjacent tissues. An increase in local temperature is more suggestive of a malignant lesion than of a benign lesion.

Mobility of a mass is of great help in ascertaining its nature. When the mass is fixed, it is either attached to bone or intraosseous. An osseous tumor is unaffected by muscle contraction. Intramuscular tumors are usually mobile when the muscle is relaxed and become fixed when the muscle is contracted. Deep, mobile lesions that are unaffected by muscle action are beneath the deep fascia and extramuscular. Tumors that are superficial and that can be moved about have not invaded deep fascia and are likely benign.

Tenderness on palpation indicates an active process and is due to an inflammatory response. An abscess or infection is very painful and is usually accompanied by other signs of inflammation, such as erythema, edema, lymphangitis, and adenopathy, whereas moderate tenderness is indicative of an active neoplastic process and the absence of tenderness suggests a quiescent lesion. One should, however, be wary, because rapid growth and necrosis of a malignant tumor may mimic infection. This may be a problem for example, in distinguishing between Ewing's sarcoma and osteomyelitis. When a rapidly growing malignant tumor is subcutaneous, it may cause vascular dilation, increased local heat, and skin turgor; such a tumor may be mistaken for thrombophlebitis or an infectious process. A neoplastic inflammatory response, however, is characterized by a firmer feel and lack of local pitting edema, and the cutaneous tissue is not as red as in infection. Point tenderness is indicative of lesions such as osteoid osteoma, a neural, or a glomus tumor. Joint range of motion may be limited because of muscle spasm or mechanical interference. There may be reactive synovitis when the lesion is adjacent to a joint or if the joint is directly involved. Muscle atrophy is not uncommon, and an antalgic limp may be present.

A vascular tumor is suspected if elevation or steady, firm pressure causes a diminution in its size, if the size is increased by the use of a venous tourniquet, or if a thrill or palpable pulsation is present. A pathologic fracture may occur in primary or metastatic malignant tumors, or one may

complicate a benign process such as a unicameral bone cyst.

Invasion of a nerve will cause neurologic symptoms and signs such as stabbing pain, paresthesia, hypoesthesia, or motor weakness. Pathologically, the nerve may be encased by the lesion or trapped against bone or rigid fascia. Neurologic dysfunction is uncommon except when tumors are in anatomic areas where nerves are unable to move freely, such as the sciatic notch or neural foramina.

IMAGING

Evaluation of the Initial Radiograph. The initial radiographic study of a lesion in bone should be evaluated systematically, with the examiner considering first the character of the lesion itself, the reaction of the surrounding bone, the location of the lesion, and the possibility of lesions in other sites.

Anatomic Site of the Lesion. The location of a bony lesion is an important diagnostic clue (Table 36–1). Epiphyseal lucent lesions are usually either chondroblastoma, infection, or occasionally eosinophilic granuloma. Epiphyseal lesions after growth plate closure are usually giant cell tumors. The metaphysis is a common site for benign tumors, unicameral cysts, osteoid osteomas, and osteosarcomas. Diaphyseal lesions include fibrous dysplasia, Ewing's sarcoma, and adamantinoma.

The portion of the skeleton involved is of diagnostic importance. Anterior vertebral lesions in children are usually eosinophilic granulomas or infection, while posterior element lesions are often aneurysmal bone cysts or osteoid osteomas. Pelvic lesions are often Ewing's sarcoma or fibrous dysplasia.

Character of the Lesion. A lesion in bone may be completely radiolucent, suggesting a cystic disorder; may have a soft tissue density; or may have bony or calcific density. Ossification within a lesion has some elements that resemble mature bone, while calcifications are usually more haphazard and of greater density. Some lesions, such as fibrous dysplasia, alter the bony architecture so that the cortices become indistinct and the bony trabecular pattern is replaced by a ground-glass appearance. A soft tissue mass adjacent to a bony lesion suggests malignancy.

Reaction of Surrounding Bone. Often the nature of a bony lesion is clear from the response of the adjacent bony tissue. A benign process such as a unicameral bone cyst has a sharp margin between the cystic cavity and the adjacent bone. The cortex is thinned and expanded, suggesting gradual enlargement from a pressure phenomenon. An irritative lesion such as an osteoid osteoma produces a vigorous response of bone formation and cortical thickening in adjacent areas. Eosinophilic granulomas produce punched-out lesions with no host reaction. Malignancies may be permeative without evident margins between the tumor and surrounding bone. When a tumor breaks through a cortex, it elevates the adjacent periosteum, resulting in new bone formation along that cortex. The apex of this elevation is seen as a triangle of periosteal bone formation, the so-called Codman's triangle. A large area of periosteal bone formation is termed a "sunburst" pattern. These periosteal reactions

TABLE 36–1 **Common Anatomic Sites of Primary Bone Tumors**

Location	Bone Tumor
Spine	
Posterior elements (spinous process, lamina, pedicles)	Aneurysmal bone cyst Osteoma Osteoblastoma
Anterior elements (vertebral body)	In a child Histiocytosis X ("vertebra plana") Hemangioma In an adult Metastases Multiple myeloma Paget's disease Hemangioma Chordoma
Long bones	Physis open
Epiphysis	Chondroblastoma Eosinophilic granuloma (epiphyseal osteomyelitis)*
Metaphysis	Multiple of benign lesions such as unicameral bone cyst Common site for osteogenic sarcoma
Diaphysis	Fibrous dysplasia Histiocytosis X Ewing's sarcoma Osteoblastoma Adamantinoma Lymphoma
Parosteal	Myositis ossificans* Osteosarcoma Chondrosarcoma Enchondroma
Ribs	In children and adolescents Fibrous dysplasia Ewing's sarcoma Metastases In adults Ewing's sarcoma Chondrosarcoma Fibrous dysplasia Multiple myeloma Metastases
Pelvis	In children Ewing's sarcoma Fibrous dysplasia Aneurysmal bone cyst Osteoblastoma In adults Ewing's sarcoma Chondrosarcoma Paget's disease Multiple myeloma Metastases
Scapula	Ewing's sarcoma Osteoblastoma Aneurysmal bone cyst
Multiple lesions	In children Multiple hereditary exostoses Fibrous dysplasia (Albright's) Histiocytosis X Enchondroma (Ollier's) Multiple hemangiomatosis Metastases-neuroblastoma, hypernephroma Lymphoma In adults Multiple myeloma

*Not a tumor.

are indicative of aggressive processes, which may occur with benign tumors and infections as well as malignancies.

Staging Studies. Staging studies are studies that define the location, extent, activity, and likely treatment of musculoskeletal lesions. Obviously benign lesions (a term to be used cautiously) may be treated based on plain radiographs alone. Examples include unicameral cysts, osteochondromas, and fibrous dysplasia. Any lesion that could be malignant should be staged before biopsy is performed.[11] One reason for this order is that biopsy may alter the findings on later studies. As mentioned previously, the plain radiograph offers the greatest amount of information at the lowest cost and inconvenience, and it should be carefully evaluated before further studies are ordered.

Computed Tomography. CT is a vital tool for determining the character and boundaries of bony lesions.[1,3,13] The extent of tumor within the bone may be accurately determined with CT.[10] Soft tissue masses may also be evaluated for size, location, and relationship to bone. Although MRI has supplanted CT for soft tissue imaging, CT remains the best modality for evaluating cortical disruption and fractures.

Magnetic Resonance Imaging. MRI is almost indispensable in the staging of tumors of the musculoskeletal system. Soft tissue lesions are demonstrated in exquisite detail, and the relationship of surrounding structures is clearly evident.[9,14] In many instances MRI is superior to CT in demonstrating the extent of tumor involvement within a long bone.[2,6,13,15] Skip lesions within the bone might be seen only with MRI. Gadolinium-enhanced imaging is often used to assess tumor necrosis secondary to chemotherapy.

Scintigraphy. Technetium scanning is used to demonstrate bone formation and blood flow, and it demonstrates bone lesions nonspecifically. Scintigraphy is more sensitive and more cost-effective for demonstrating bone metastases than plain radiography. A normal scan strongly suggests that a lesion is benign, but an abnormal scan cannot distinguish a benign from a malignant lesion.[12] Benign tumors that affect more than one bone may be evaluated with this modality. Benign lesions that are "hot" on scan include osteoid osteoma, osteoblastoma, aneurysmal bone cyst, and fibrous dysplasia. "Cold" lesions include eosinophilic granuloma and myeloma. Intraoperative scintigraphy may be used to locate osteoid osteoma lesions.

Gallium scintigrams are obtained to evaluate soft tissue tumors. Sarcomas usually cause increased uptake of gallium, while noninflammatory benign tumors have normal uptake.[7]

Angiography. Angiography is not commonly used in tumor staging today because of the information available noninvasively using MRI. When detailed study of the vasculature is necessary in planning a limb-sparing procedure, angiography may be necessary. Also, angiography is used when a lesion is to be embolized prior to treatment to decrease vascularity. At times angiography is used to instill cytotoxic agents directly into the vasculature of the tumor.

BIOPSY

A biopsy is required in treating all malignant tumors, and in many cases it is necessary in managing benign lesions. Radiographic diagnoses without biopsy are often safely made for a variety of benign lesions, including unicameral bone cyst, aneurysmal cyst, fibrous cortical defect, fibrous dysplasia, chondroblastoma, osteochondroma, and osteoid osteoma. When there is a suspicion of malignancy, a tissue diagnosis is required. When the appearance of the lesion is typical for a certain diagnosis and all staging studies support that diagnosis, a biopsy may be done as part of the definitive surgical procedure. In all other cases an incisional biopsy prior to treatment is recommended.

TABLE 36–2 **Enneking Classification of Sarcomas of Bone or Soft Tissue**

Stage	Grade	Site	Metastases
IA	Low	Intracompartmental	None
IB	Low	Extracompartmental	None
IIA	High	Intracompartmental	None
IIB	High	Extracompartmental	None
III	Low or high	Intra- or extracompartmental	Yes

*From Enneking W, Spanier S, Goodman M: A system for the surgical staging of musculoskeletal sarcoma. Clin Orthop 1980;153:106.

The rules of biopsy for musculoskeletal lesions have been well established for a number of years, yet poorly done biopsies continue to cause harm to patients. In most cases the biopsy of a likely malignant lesion should be deferred to the individual who is capable of definitively treating that patient. Bad biopsies can preclude the use of limb salvage and may increase the risk of tumor recurrence and death. To quote Enneking, "The optimal chance for an adequate local procedure is in the virgin, unbiopsied state."[4]

Needle biopsies are often used, and in centers with appropriate expertise they often provide definitive diagnoses. At times they are done in radiology suites with CT guidance. The volume of tissue obtained is limited, and pathology and radiology consultations should be obtained before biopsy.[8]

Open incisional biopsies are most often used for bone and soft tissue sarcomas. The incision should be longitudinal and placed so that the incision tract can be completely excised at the time of tumor excision without undue compromise of function. Hemostasis must be meticulous, as bleeding into the tissues spreads tumor. Retraction also must be gentle; sharp rakes can spread tumor cells. Closure of each compartment should be complete and a bone plug may be reinserted or replaced with methacrylate to seal the bone.[4,8] Prior to biopsy the surgeon should consult radiolo-

TABLE 36–3 **Types of Excision of Tumor as Related to Surgical Margins***

Type	Plane of Dissection	Result
Intralesional	Debulking or curettage	Leaves macroscopic disease
Marginal	Pericapsular reactive zone	Likely to leave microscopic disease
Wide	Normal cuff of tissue (intracompartmental)	May leave "skip" or "satellite" disease
Radical	Whole bone or muscle outside compartment (extracompartmental)	No residual

*Needs surgical *and* pathologic verification.

gists and pathologists so that the biopsy produces the most diagnostically useful tissue.

CLASSIFICATION

Benign tumors are classified as latent, active, or aggressive. A latent benign tumor (stage 1) is intracapsular, is usually asymptomatic, and never metastasizes. An active benign tumor (stage 2) is also intracapsular and rarely metastasizes but is actively growing and often symptomatic. An aggressive benign tumor (stage 3) often breaks through its capsule and extends into an adjacent compartment. Rarely, these may metastasize.[11]

Enneking has classified sarcomas of bone and soft tissue into various stages according to the grade of the histology, the location of the tumor relative to anatomic compartments, and the presence of metastases. A low-grade tumor has well-differentiated cells, few mitotic figures, few or no atypical cells, little necrosis, and no vascular invasion. High-grade tumors have frequent mitoses, are poorly differentiated, have atypical cells, necrosis, little matrix, and show vascular invasion.

The ability to treat malignant tumors successfully with limb salvage depends on understanding sarcoma behavior. "A sarcoma grows centrifugally like a spreading ripple on a pond. However, as it expands it follows the path of least resistance."[4] If a tumor remains within its compartment, either osseous or fascial, it can be removed successfully by resecting the entire compartment. A bone is considered to be a compartment, as is a muscle or a joint. Tumors may invade into adjacent compartments and become extracompartmental. The Enneking staging system is shown in Table 36–2.

As tumors grow they compress surrounding tissues into structures that resemble fibrous capsules. This surrounding tissue contains tumor cells, known as satellites. In addition, there may be tumor cells in surrounding normal tissues, called skips.[4] Within a bone there may also be skip metastases, with intramedullary tumor extending well proximal to the apparent extent of the primary tumor.

TREATMENT

The treatment of tumors of the musculoskeletal system should be undertaken only by surgeons who possess understanding of and training in the basic principles of tumor management. The margins of excision are vitally important, to give the patient the best chance of curing the disease (Table 36–3).

An intracapsular margin of tumor removal leaves gross tumor behind and is appropriate only for certain benign lesions. An example is curettage of an aneurysmal bone cyst.

A marginal excision is done by removing the tumor and its pseudocapsule. Because the capsule contains tumor cells, this excision by definition leaves viable tumor in the surrounding local tissues. This excision is inadequate for local removal of a malignancy.

A wide margin is defined as one that is free of tumor. This requires removal of tissue beyond the reactive pseudocapsule so that a cuff of normal tissue surrounds the tumor and capsule. This is sufficient for the primary tumor, but intracompartmental skip lesions may remain.

A radical margin implies removal of the primary lesion and all normal tissue within the compartment. This surgery ensures removal of the tumor and any skip or satellite lesions.[4]

Whenever possible, limb-sparing procedures are preferred, but the surgeon must adhere to the principles of tumor excision. Amputations often achieve a radical margin and are necessary when limb sparing cannot be safely performed. The principles of compartment involvement and staging apply equally to amputations as to limb salvage surgery.

REFERENCES

1. Berger P, Kuhn J: Computed tomography of tumors of the musculoskeletal system in children. Radiology 1978;127:171.
2. Bloem JL, Taminiau AH, Eulderink F, et al: Radiologic staging of primary bone sarcoma: MR imaging, scintigraphy, angiography, and CT correlated with pathologic examination. Radiology 1988;169:805.
3. De Santos L, Goldstein H, Murray J: Computed tomography in the evaluation of musculoskeletal neoplasms. Radiology 1978;128:89.
4. Enneking W: Principles of musculoskeletal oncologic surgery. In Evarts C (ed): Surgery of the Musculoskeletal System. New York, Churchill Livingstone, 1990.
5. Enneking W, Spanier S, Goodman M: A system for the surgical staging of musculoskeletal sarcoma. Clin Orthop 1980;153:106.
6. Gillespy T, Manfrini M, Ruggieri P, et al: Staging of intraosseous extent of osteosarcoma: correlation of preoperative CT and MR imaging with pathologic macroslides. Radiology 1988;167:765.
7. Kirchner P, Simon M: The clinical utility of bone and gallium imaging of soft tissue sarcomas of the extremities. J Bone Joint Surg 1984;66-A:319.
8. Murray J, Mankin H: Biopsy technique in musculoskeletal tumors. In Evarts C (ed): Surgery of the Musculoskeletal System, vol 5. New York, Churchill Livingstone, 1990.
9. Petasnick J, Turner D, Charters J: Soft tissue masses of the locomoter system: comparison of MR imaging with CT. Radiology 1986;170:125.
10. Schreiman JS, Crass JR, Wick MR, et al: Osteosarcoma: role of CT in limb-sparing treatment. Radiology 1986;161:485.
11. Simon M: Diagnostic and staging strategy for musculoskeletal tumors. In Evarts C (ed): Surgery of the Musculoskeletal System. New York, Churchill Livingstone, 1990.
12. Simon M, Kirchner P: Scintigraphic evaluation of primary bone tumors: comparison of technetium 99m phosphonate and gallium citrate imaging. J Bone Joint Surg 1980;62-A:758.
13. Sundaram M, McGuire MH: Computed tomography or magnetic resonance for evaluating the solitary tumor or tumor-like lesion of bone? Skeletal Radiol 1988;17:393.
14. Totty W, Murphy W, Lee J: Soft tissue tumors: MR imaging. Radiology 1986;1960:135.
15. Vanel D, Verstraete KL, Shapeero LG: Primary tumors of the musculoskeletal system. Radiol Clin North Am 1997;35:213.