Problems in Family Practice

Evaluation and Treatment of Bone Tumors

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The family physician will rarely see patients with bone tumors; however, when bone tumors do arise, they can be devastating as they unfortunately occur in young patients and are among the most malignant of lesions. The diagnosis of a bone tumor should be suspected if there is deep aching pain, a mass, or a pathological fracture. X-ray films usually lead to the diagnosis and help distinguish malignant from benign lesions. Benign tumors are relatively small, do not break out of the bone, and leave the cortex intact and the soft tissue uninvolved. Malignant tumors are large, break out of the bone, and involve the soft tissues. In general, benign tumors are treated with biopsy, local excision, or curettage with bone grafting. Malignant tumors require much more extensive surgery including wide radical excision (probably amputation), chemotherapy, and/or radiation therapy as indicated.

As in any other system in the body, tumors arise in the skeletal system. These tumors may arise within the skeleton as primary growths or may spread secondarily to the skeleton from some distant primary location. Bone tumors are less common than tumors of other organ systems; however, they are among the most malignant of lesions and are, unfortunately, found in young patients.

It is imperative that the diagnosis of a bone tumor be made early and with absolute accuracy so that the definitive treatment can be planned with extreme care. Accurate tissue identification may prove quite difficult. Some tumors may be borderline malignant-benign, making the prognosis questionable. This difficulty arises frequently with the cartilage tumors and giant cell tumors. The biologic behavior of some tumors may also be difficult to predict from their histologic appearance. A tumor that appears benign by most criteria may occasionally behave in an aggressive or malignant manner, while a tumor identified as malignant may be quite limited in its progression.

A primary bone tumor (Table 1) is a neoplasm arising from any one of the elements comprising bone as a tissue.[1] A secondary neoplasm or metastatic tumor is a lesion that has spread to bone from another site. Most neoplasms of bone are found near the metaphyseal area, and over 80 percent of primary tumors are either in the distal femur or proximal tibia.[2] These areas have tremendous growth activity and, therefore, are more likely to develop a neoplasm. One can also use the same reasoning to explain why most bone tumors are found in growing children.

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Table 1. Classification of Bone Tumors

Tissue of Origin	Benign	Malignant
Bone	Osteoid osteoma Osteoblastoma	Osteogenic sarcoma
Cartilage	Osteochondroma Enchondroma Chondroblastoma Chondromyoid fibroma	Chondrosarcoma
Fibrous tissue	Fibrous cortical defect Nonossifying fibroma Fibrous dysplasia Desmoplastic fibroma	Fibrosarcoma Malignant fibrous histiocytoma
Fat	Lipoma	Liposarcoma
Notochord	None	Chondroma
Vascular tissue	Hemangioma	Angiosarcoma
Marrow elements	None	Ewing's sarcoma Myeloma Reticulum cell sarcoma
Uncertain origin	Giant cell tumor Aneursymal bone cyst Solitary bone cyst	Adamantinoma

Table 2. Radiographic Differentiation of Malignant and Benign Bone Tumors*

	Benign	Malignant
Size	Small	Large
Bone reaction	Sclerotic border	Ill-defined border
Bone confinement	Cortex intact	Broken out of cortex
Soft tissue involvement	None	Soft tissue mass present
Location	More likely to be distal	More likely to be axial

*X-ray diagnoses are difficult. These are guidelines and are *not* to be considered pathognomonic characteristics

Recognition

The symptoms and signs of bone tumors vary. As a rule, the patient seeks medical advice because of one or more of the three common manifestations of bone tumors: pain, a mass, or a pathological fracture. The first evidence of almost all malignant and several benign tumors is pain. It is usually of a deep, aching character, often most disturbing at night. Absence of pain usually indicates that a bone lesion is benign. Sometimes the patient first notices a mass, which may or may not be painful. Occasionally, a pathologic fracture

brought on by minor exertion is the first indication of a tumor. An asymptomatic, unsuspected neoplasm may be discovered in a routine roentgenogram or when an x-ray film is taken for an unrelated reason and the part is included fortuitously.

X-ray studies usually lead to the diagnosis. The tumors are recognized by an alteration in the contour of the cortex, a change in the trabecular pattern, a lytic area (hole in bone), and/or sclerotic (increased density) area. In some instances, the clinical and roentgenographic features of a bone lesion are so characteristic that a film diagnosis can be made without additional study. This is true for osteochondroma (Figure 1) and the nonossifying fibroma (Figure 2). In general, there are great similarities in x-ray appearance between various tumors, making the absolute diagnosis difficult. The cells which participate in the response to injury or disease originate from the osteoprogenitor cells (pluri-potential cells). Therefore, there is only a limited spectrum of responses possible regardless of the nature of the disease or injury (Figure 3). The responses of the bone cause the x-ray appearance of various different lesions to be quite similar making the diagnosis a challenging, if not sometimes impossible, task.

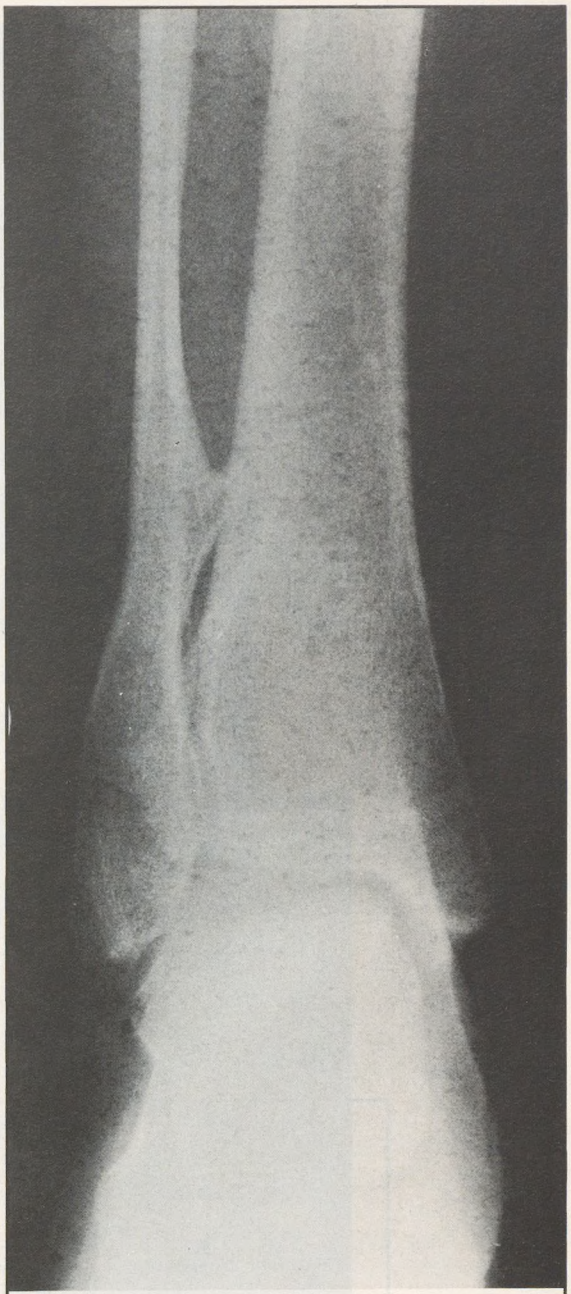

Figure 1. Osteochondroma of the fibula proximal to the ankle

Benign or Malignant?

Primary bone tumors may be benign or malignant. To the clinician and patient, the potential for malignancy is the most important feature of any tumor and should be determined as soon as possible. Benign tumors are generally slow growing, well-circumscribed, non-invading tumors that cause few symptoms, do not spread or metastasize, and do not cause the death of the patient. Malignant bone tumors grow rapidly, spread, expand, invade irregularly, and are associated with pain and disability. They spread or metastasize to the lungs and other tissues, bringing about rapid death. Any hope for survival depends upon early diagnosis and adequate aggressive treatment.

The roentgenogram remains the major diagnostic tool to distinguish malignant from benign bone tumors. Unfortunately, there are no pathognomonic characteristics of malignant and benign tumors, but there are some guidelines (Table 2) that can be used to help in the differential diagnosis. Generally, benign tumors are small relative to the

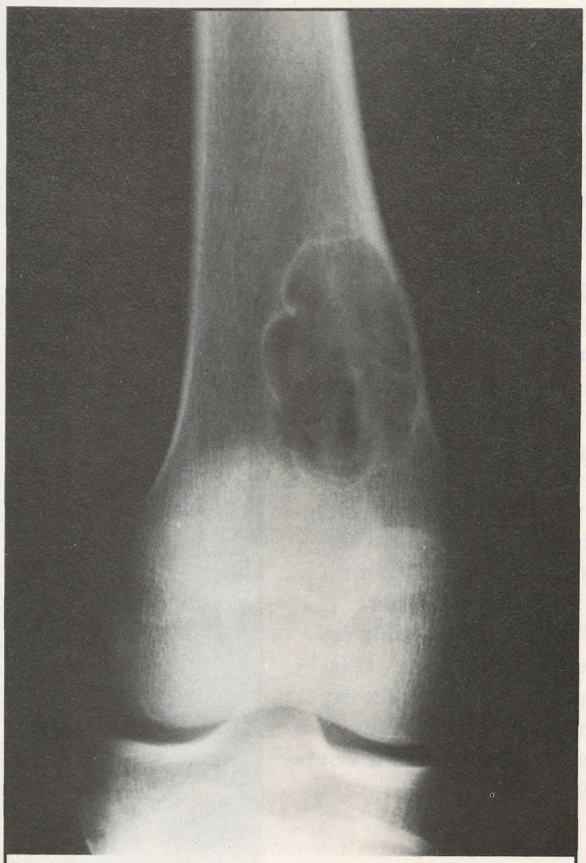

Figure 2. Nonossifying fibroma of distal femur

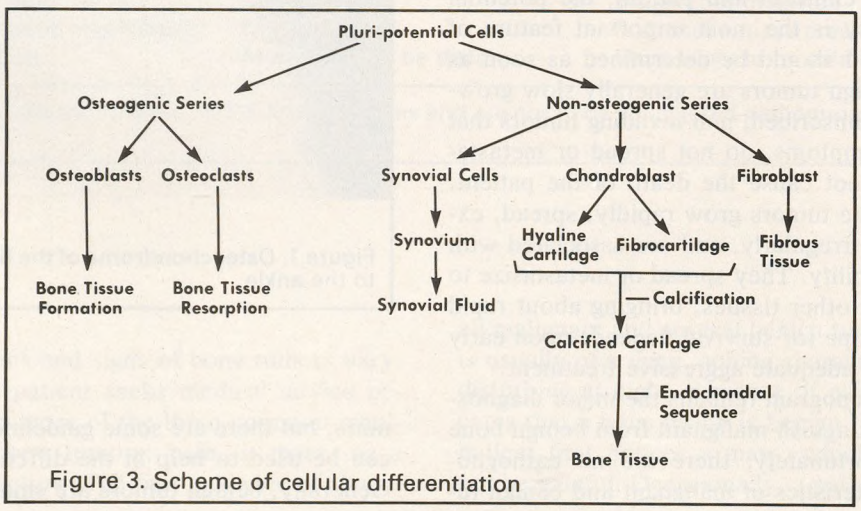

Figure 3. Scheme of cellular differentiation

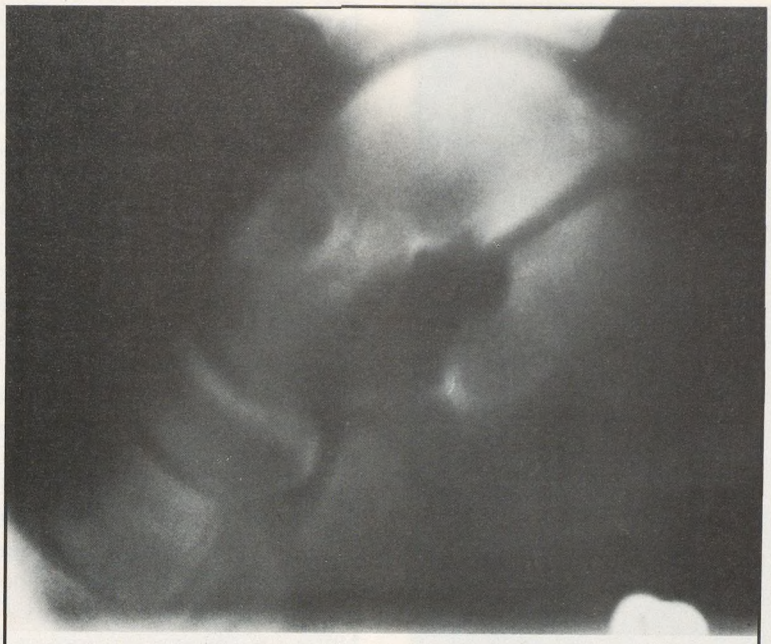

Figure 4. Osteoid osteoma of the talus. Note the lytic lesion with the sclerotic border

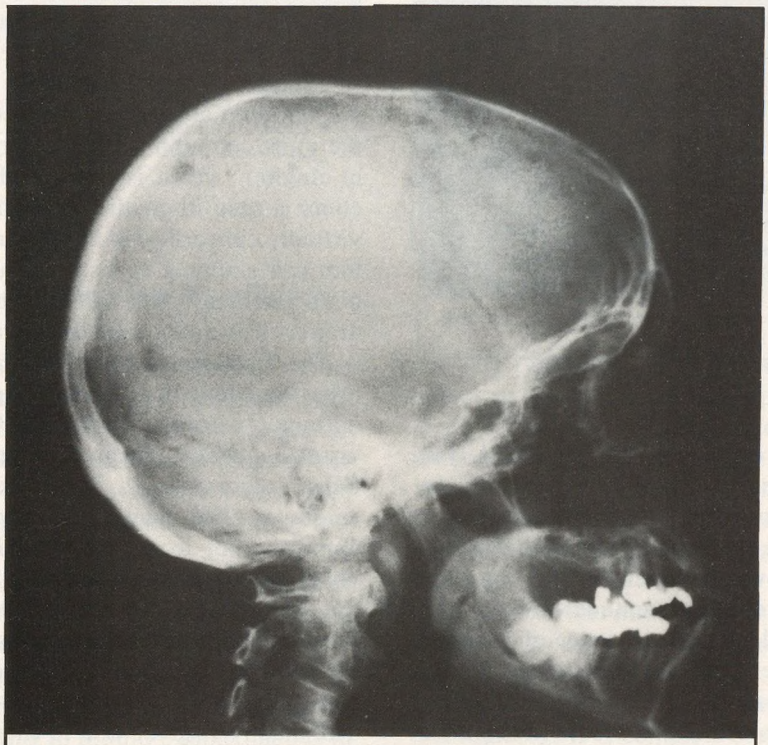

Figure 5. Multiple myeloma. Note the multiple small lytic lesions in the skull

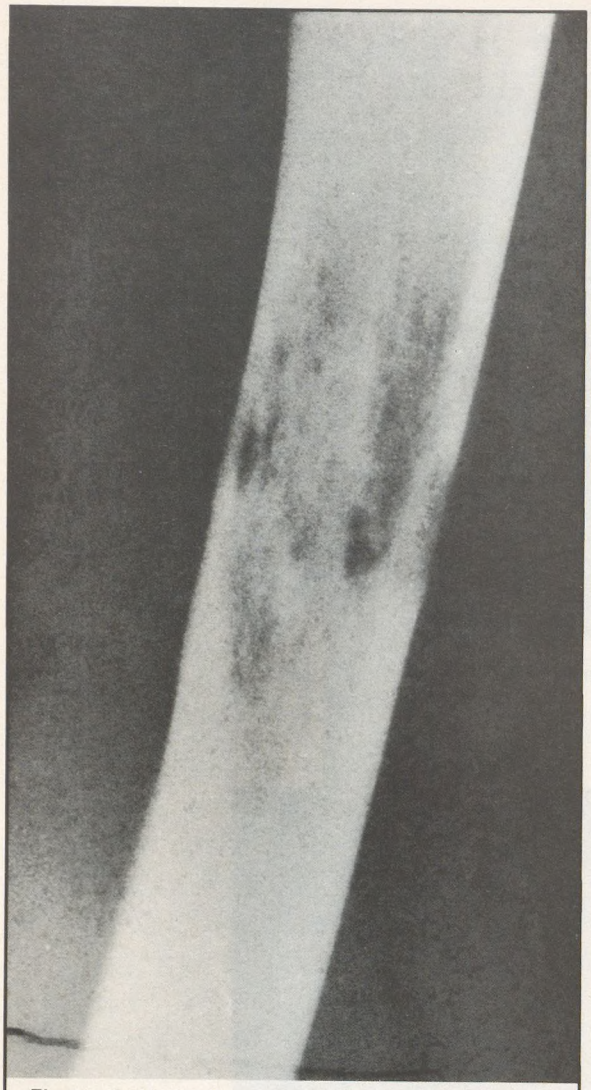

Figure 6. Ewing's sarcoma in diaphysis of the femur

size of the bone in which they are located. A lytic tumor 1 cm in diameter located in the second cervical vertebra is more ominous than a 3 cm lesion in a large bone like the femur. Benign tumors are generally slow growing; therefore, the bone has sufficient time to react and remodel in response, producing a well demarcated border of sclerotic bone as seen in osteoid osteoma (Figure 4). Benign tumors do not break out of the bone but rather leave the cortex intact and the soft tissue uninvolved. The location of the tumor (especially cartilage tumors) is important as benign tumors are more likely to be distal to the axial skeleton. Malignant tumors, on the other hand, are more likely to be axial in location and large, to break out of the bone, and to involve the soft tissues. These tumors grow rapidly, not giving the bone a chance to respond with reactive new bone formation.

The x-ray film displays the end result of the response of bone tissue and the destruction created by the tumor.[3] When bone destruction predominates, patterns of lysis can be identified that are useful in the radiographic diagnosis of the type of bone tumor. Tumors of marrow origin have a characteristic "moth-eaten" pattern as seen in multiple myeloma (Figure 5), reticulum cell sarcoma, or Ewing's sarcoma (Figure 6). Large lesions with a "geographic" pattern of destruction are typically seen in aggressive giant cell tumors (Figure 7), fibrosarcomas (Figure 8), and osteosarcomas (Figure 9).[4] Periosteal bone reaction or new bone formation is an ominous sign for malignancy, but is not specific for primary bone tumors.[5] The presence or absence of calcification or ossification within the lesion can be helpful in identifying cartilage tumors or tumors of osseous origin. The x-ray pattern, however, must be correlated with the biopsy microscopic features, as x-ray studies alone are unlikely to give an accurate diagnosis.

The age of the patient can be of some help with the differential diagnosis. Osteogenic sarcoma is the most common malignant primary bone tumor in children, yet it is rare in adults. Ewing's sarcoma is seen in children and the young adult but virtually unheard of in middle and old age. Reticulum cell sarcoma is histologically similar to Ewing's sarcoma but is virtually never seen in children as it is a tumor of middle and old age.

The location of the tumor within the bone can offer some help in differentiating the various types of bone tumors (Figure 10). Chondroblastomas virtually always arise in the epiphysis of the bone. Other tumors rarely, if ever, arise solely in the epiphysis. The giant cell tumor may involve the epiphysis but a portion will virtually always involve the adjacent metaphysis. The metaphysis is the site of origin of numerous tumors including osteosarcoma, fibrosarcoma, chondrosarcoma, giant cell tumor, osteoblastoma, chondromyofibroma, nonossifying fibroma, and unicameral bone cysts. The diaphysis gives rise to the round cell tumors such as Ewing's sarcoma and reticulum cell sarcoma.

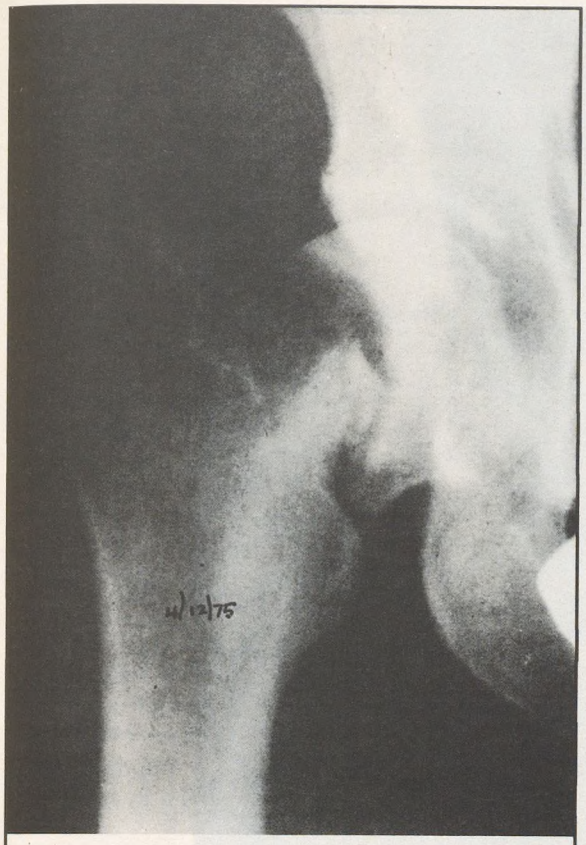

Figure 7. Giant cell tumor of greater trochanter and neck of femur. Note the pathological fracture

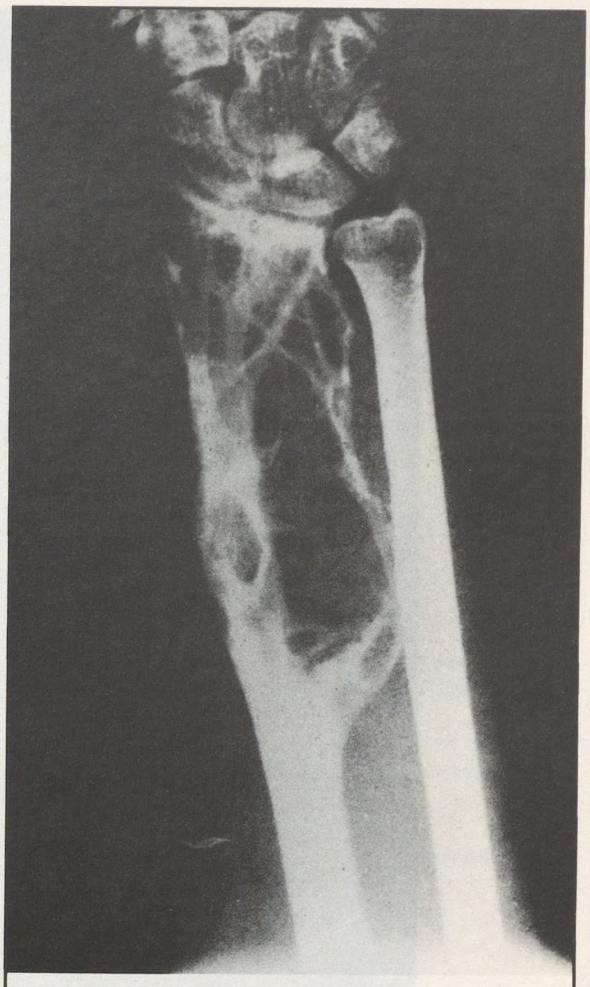

Figure 8. Fibrosarcoma of distal radius

Role of the Family Physician: Pre-Biopsy Evaluation

The role of the primary care physician is to recognize the presenting signs and symptoms and order the initial x-ray studies to identify the patient with the bone tumor. Consultation with the radiologist and orthopedic surgeon should be expedited and the potential for a malignant or locally destructive process be determined.

If the process is benign, such as unicameral bone cyst, nonossifying fibroma, enchondroma, exostosis, chondroblastoma, or chondromyofibroma, the generally accepted treatment is biopsy to confirm the diagnosis, and local excision or curettage with bone grafting to promote rapid healing in order to regain the integrity of the bone. Occasionally, for very small asymptomatic lesions that are very typically benign such as a fibrous cortical defect or exostosis, the orthopedic surgeon may elect to observe the patient over a period of time without a biopsy. In these cases, the patient must be reliable and understand the importance for close follow-up and repeat x-ray studies at intervals, checking for changes in size or contour of the lesions.

If, on the other hand, there is any potential for a locally aggressive or malignant tumor, the pre-biopsy work-up (Table 3) is crucial and should be started with consultation of an orthopedic surgeon and radiologist. A complete blood count and sedimentation rate are performed to rule out infection. An osteomyelitis can mimic a malignant osteo-

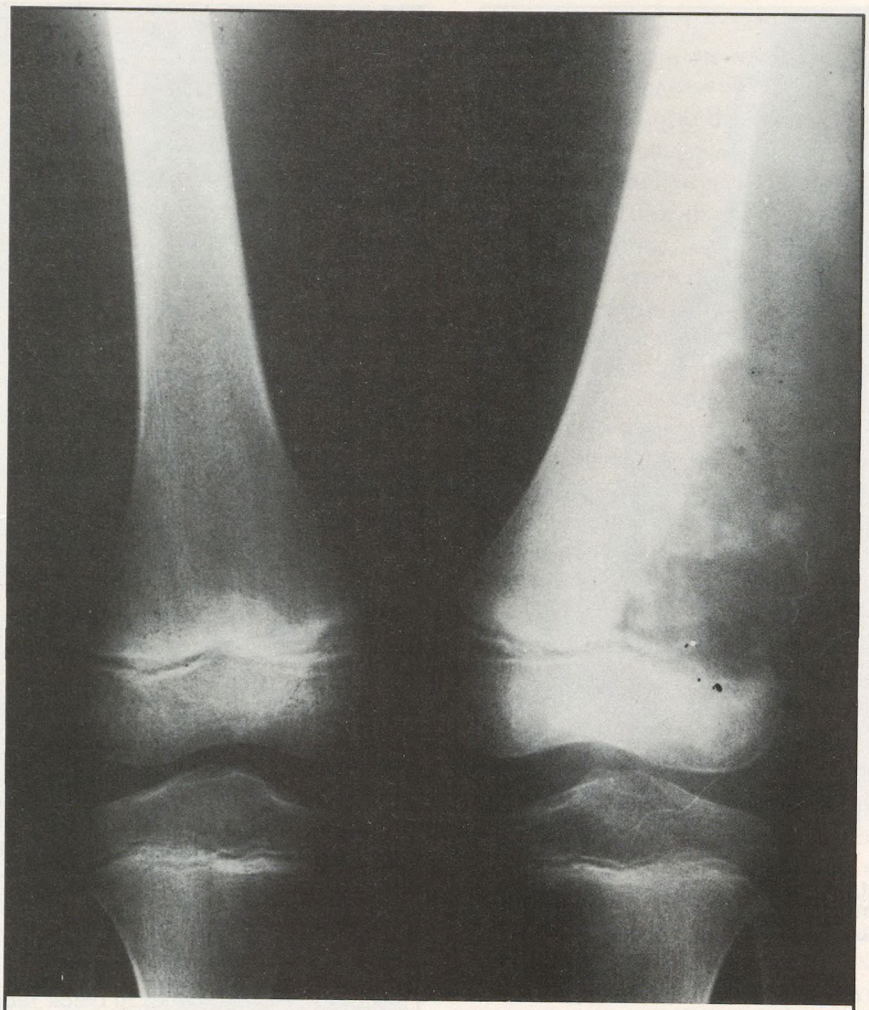

Figure 9. Osteosarcoma of distal femoral metaphysis

sarcoma and must be ruled out. A Brown tumor of hyperparathyroidism can be ruled out with calcium, phosphorus, and alkaline phosphatase studies.

An immunoglobulin electrophoresis is obtained in adults to confirm or rule out multiple myeloma. Malignant bone tumors generally will metastasize first to the lungs and, therefore, a full lung tomogram or Computerized Axial Tomography (CAT) scan is done. The bone scan is important not only to determine the activity of the lesion in question but also to see if there are other skeletal lesions. Tomograms of the lesion are obtained to determine the extent of the bony involvement and to look for possible calcification (indicating a cartilage tumor) or ossification (indicating a tumor of bone origin).

Prior to biopsy, the orthopedic surgeon must consider the various treatment options for each of the possible lesions with which he may be dealing. An assessment therefore must be made, before the biopsy, of the soft tissue involvement. The soft tissue extent of the tumor can only be determined by an arteriogram or CAT scan. It is essential that this be done prior to the biopsy, as the biopsy itself may distort the soft tissues, making an assessment of their involvement impossible.

After the above studies are completed, the

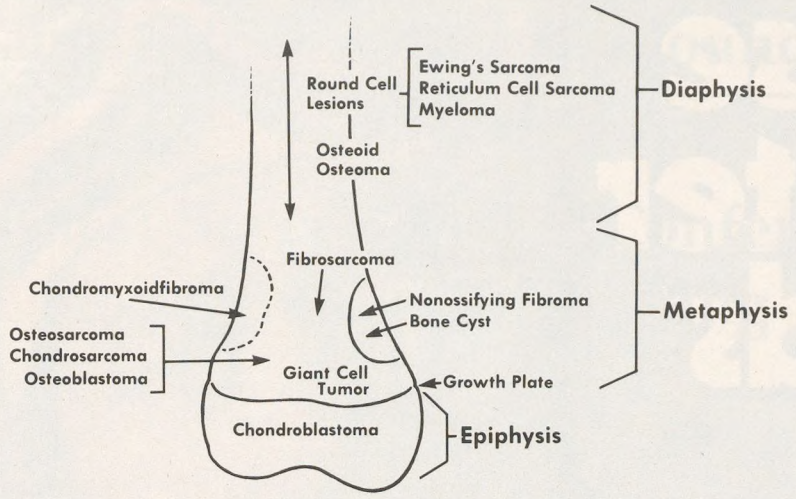

Figure 10. Common locations of various tumors within a bone

biopsy can be performed. Usually an incisional biopsy is recommended, closing the wound and waiting for permanent sections for the diagnosis. Rarely should a definitive diagnosis be made on the basis of a frozen section.

Principles of Treatment

In general, benign tumors are treated with biopsy, local excision, or curettage with bone grafting. Malignant tumors require much more extensive surgery including wide radical excision (probably amputation), chemotherapy, and/or radiation therapy as indicated. Presently, aggressive bone tumors like osteosarcoma are treated surgically with amputation along with adjuvant chemotherapy. Great advances have been made with the chemotherapy of osteosarcomas, with the reports of up to 60 percent five-year survival rates.[6]

Obviously, these malignant tumors are devastating to the patient and family members. The ultimate success of treatment depends upon the cooperation of the various specialists including the radiologist, pathologist, chemotherapist, orthopedic surgeon, and family physician. Each patient with his/her tumor must be treated individually and given the benefits of the most up-to-date treatment protocol which usually requires a treatment team approach. Usually such an approach is best handled in larger medical centers where these specialties are readily available.

Table 3. Pre-biopsy, X-ray, and Laboratory Evaluation

Complete blood count, Sedimentation rate
Calcium, Phosphorous
Alkaline phosphatase
Immunoglobulin electrophoresis (adults)
Chest x-ray studies
Chest tomograms and/or CAT scan
Tomograms of lesion
Bone scan
Arteriogram and/or CAT scan of lesion

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