Clinicopathological Conference:* Painful Leg Mass in a 23-Year-Old Male

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Clinical History

A 23-year-old Negro male truck driver was admitted to the MCV Hospitals on 1-4-66 because of "swelling" of his right leg and "pain" of recent onset. He said he had hit his right leg just below the knee in early 1962, but had had little trouble with the leg until he jumped from a moving truck in July of that year, when he noted pain and the leg became swollen. He spent 24 hours in the dispensary with the leg immobilized. X-rays were said to be negative. The patient stated that approximately a year before this admission the leg was examined, x-rays were taken, and he was told "there was nothing to worry about." The leg had gradually increased in size, but there had been only a slight amount of pain and no increased heat in the affected area. Just before admission he complained of pain and numbness over the dorsum of the right foot.

Past medical history and family history were negative. Review of systems was noncontributory.

Physical examination: Blood pressure 120/60, pulse 76/min, respiration 20 breaths/min, temperature 98.6°. The patient was a well-developed, well-nourished, young man in no acute distress. The pertinent findings were limited to the right leg where a large, firm, immovable mass was noted that extended from just below the knee to about midcalf on the lateral aspect of the leg. The skin overlying the mass was warm and tense. There was a foot drop on the right, inability to dorsiflex the great toe, weakness of dorsiflexion of the remaining toes, and decreased sensation over the dorsum of the right foot.

Laboratory data: The urine was yellow, clear, and acid with a specific gravity of 1.021. Protein, sugar, and acetone were negative. Microscopic examination of the urine sediment was negative. Hemoglobin 12.6 g/100 ml; white cell count 6,400/mm³ (60% neutrophils, 34% lymphocytes, 4% monocytes, and 2% eosinophils).

Anteroposterior and lateral x-rays of the right leg showed a large tumor involving the upper shaft of the fibula, and marked linear soft tissue calcification within the tumor which appeared to form septa. A chest film was negative.

The patient underwent surgery on 1-6-66.

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Clinical Discussion

Dr. Gerald A. Gildersleeve: The historical and physical findings in this 23-year-old Negro man are limited to the right leg and foot. His complaints date to two episodes of trauma in 1962, with apparently normal radiographs of the area in question in July of that year. Gradual swelling of the area, pain, and now deep peroneal nerve deficit have occurred.

Radiographs of the chest and abdomen are normal. Radiographs of the right leg are abnormal and show (fig. 1) an enormous, expansile, destructive lesion involving the proximal shaft and metaphyseal end of the fibula. The lesion is encased in periosteal new bone which is markedly folded, wrinkled, and absent in some areas, indicating varied degree of tumor aggressiveness in areas of the growth margins. The fairly abrupt distal junction of tumor with intact shaft shows a remarkable absence of sclerosis in the lateral view. Fascial planes are preserved close to the tumor indicating a lack of adjacent soft tissue response. The integrity of the knee joint is preserved. No calcification or ossification is appreciable within the matrix of the tumor, a rather important feature.

Before entering into specific diagnostic considerations, I shall make a few general comments concerning solitary tumor in bone.

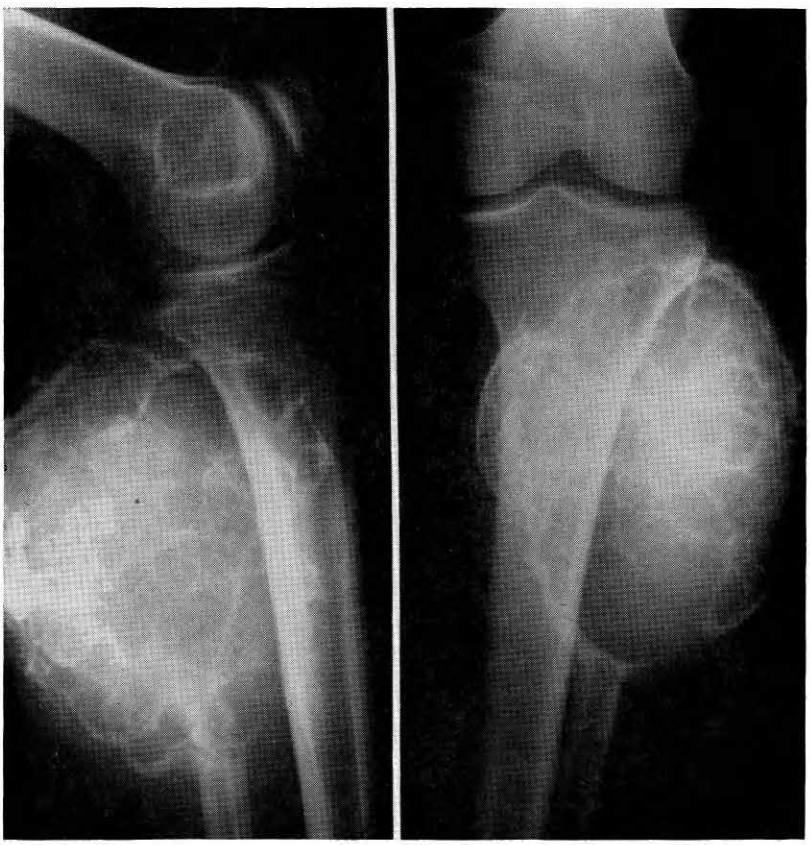

Fig. 1—Lateral and anteroposterior radiographs of the right lower leg revealed an enormous, expansile, destructive lesion involving the proximal shaft and metaphyseal end of the proximal fibula. The lesion is encased in periosteal new bone which is markedly folded, wrinkled and irregular, indicating varied degrees of tumor aggressiveness in areas of the growth margins. No calcification or ossification is seen within the matrix of the tumor.

The radiographic diagnosis of solitary bone tumors is based on a combination of findings which depend on tumor type and which may vary with response of the spongy bone, cortical bone, periosteum, and adjacent soft tissue. Some tumors produce a sufficiently consistent picture to allow accurate specific diagnosis on the basis of x-ray studies alone. Others produce varied appearances. In these the size, shape, and location of the lesion, the presence or absence of tumor matrix calcification and ossification, and the host response will limit the number of possibilities. In general, when these findings are correlated with the historical and physical findings, an accurate diagnosis should be made in at least 80% of the cases.

Metastatic lesions are more common than primary lesions of bone and, therefore, must receive consideration. Approximately 75% of metastatic lesions involve more than one area in the skeleton. They are primarily positioned in the medullary portion of marrow-containing bone (axial skeleton and proximal femur and humerus of adults), and are characterized by relative sparing of overlying cortex, lack of any degree of periosteal response, and absence of adjacent soft tissue mass. They tend to be small, about 1 to 3 cm in diameter. Though metastases from kidney and thyroid are notable exceptions, the extensive cortical destruction, large size, marked periosteal response, solitary character, and distal position of the lesion in question combined with lack of evidence of a distant primary site are all against metastatic lesions. A primary bone tumor is therefore more likely in this case.

Table 1 lists those primary bone lesions which either have no matrix calcification or ossification, or which may have no radiographically appreciable matrix calcification or ossification, and, therefore, resemble the lesion in question.

On the basis of location, size, and shape of the lesion and the age of the patient, adamantinoma, non-ossifying fibromia, chondromyxoid fibroma, chondroblastoma, and enchondroma can be eliminated.

The well-developed, folded periosteal new bone and well-defined junction of tumor and normal shaft eliminate as possibilities such highly aggressive destructive lesions as osteolytic osteosarcoma, Ewing's sarcoma, and reticulum cell sarcoma. The remaining possible primary lesions to be considered are then myeloma, fibrosarcoma, aneurysmal bone cyst, and giant cell tumor of bone.

In the excellent monograph by Dahlin and co-workers (Dahlin, Ghormley, and Pugh, 1956) in which they reviewed 2,276 cases of bone tumors, none of 140 myelomas presenting as solitary lesions occurred in the fibula. Only two occurred in the third decade of life; most were in the fifth to seventh decades.

Fibrosarcoma, a tumor of young to middle-aged adults, with a 2:1 ratio of male to female incidence, frequently involves the end of a long bone. Its usual aggressiveness does not allow the highly developed periosteal response encountered here; however, such an appearance may occur if this tumor grows slowly. It is relatively uncommon, encountered only one-third as often as giant cell tumor.

Aneurysmal bone cyst is only one-half as common as giant cell tumor. Sixty-six percent occur under age 20. The periosteal calcific shell tends to be very thin, and uniformly ballooned over the lesion. This lesion tends to show tumor matrix calcifications or ossification, which our lesion does not do.

The single remaining lesion to be considered is giant cell tumor of bone. Ninety percent of these tumors occur from age 20 on, and most between ages 20 and 35. It is classically an expansile, destructive tumor originating in the metaphyseal end of a long bone after epiphyseal closure, which respects the barrier of joint cartilage, and which elicits no sclerotic response of the adjacent spongy bone. The periosteal response is varied, depending on the rate of growth of the tumor. When various portions of the tumor grow at different rates, the periosteal new bone assumes a folded or wrinkled appearance giving a "soap bubble" appearance. No primary matrix calcification or ossification is seen on radiographs of giant cell tumors. No adjacent soft tissue inflammatory host response is elicited by giant cell tumors.

By correlation of the roentgenographic findings of size, location, shape, matrix appearance, and host response with the history and physical findings, the most likely diagnosis is giant cell tumor of bone.

Ward Diagnosis

Aneurysmal bone cyst
or ? Osteogenic sarcoma
or ? Giant cell tumor

TABLE 1
Matrix Characteristics of Some Primary Bone Tumors

No matrix calcification or ossification:
Ewings
Reticulum cell
Giant cell
Myeloma
May have no matrix calcification or ossification:
Osteolytic osteosarcoma
Enchondroma
Chondroblastoma
Chondromyxoid fibroma
Non-ossifying fibroma
Fibrosarcoma
Aneurysmal bone cyst
Adamantinoma

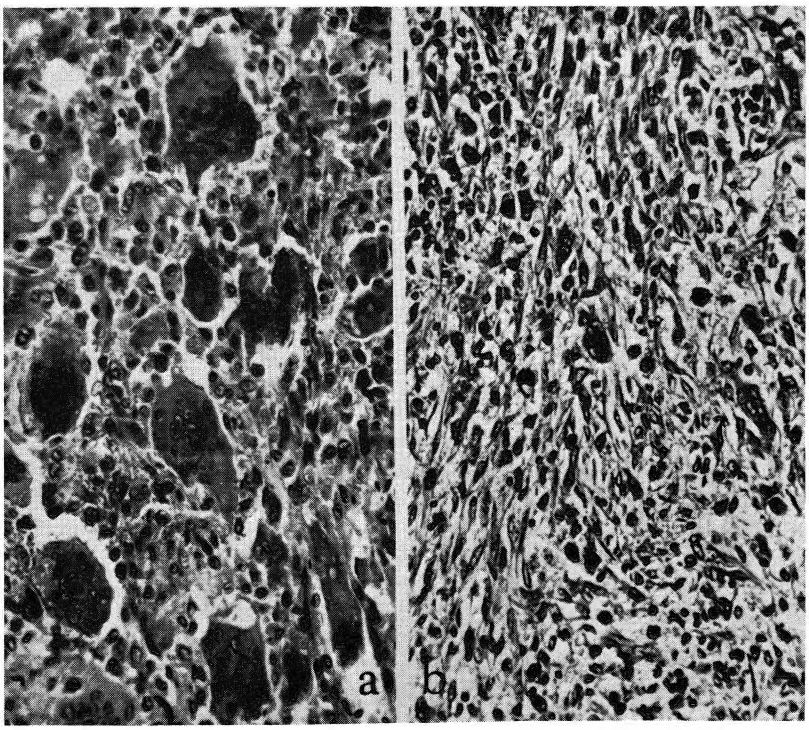

Fig. 2—Most of the tumor was composed of large, multinucleated giant cells against a background of spindly stromal cells (*a*). Typical giant cells were fewer, and mitoses more frequent in the more aggressive areas (*b*).

Dr. Gildersleeve's Diagnosis

Giant cell tumor of the fibula

Pathological Discussion

Dr. Saul Kay: The surgical specimen was received in three installments. At first we received a mass of yellowish and maroon tissue, 5 × 2.5 × 2 cm. This was sent for frozen section. Following a diagnosis of giant cell tumor, the proximal fibula was resected; this was received as a bony shell 18 × 12 × 7.5 cm covered by a small amount of muscle tissue. The bone was fractured in several places and was filled with similar soft yellowish and maroon tissue. Following confirmation of the diagnosis of giant cell tumor, the right lower extremity was amputated 17 cm above the knee six days later. The tibia showed an area of tumor invasion, 1.9 cm deep to the tibial plateau in the lateral cendyle. This area measured 2.4 × 1.3 cm, and tumor extended to the periosteal surface posteriorly.

Microscopically, the lesion was a typical giant cell tumor, described as a Grade II lesion by virtue of the presence of many plump spindle cells and occasional mitoses (fig. 2). That it was also clinically aggressive was borne out by its invasion of an adjacent bone not primarily involved and its breakthrough into the soft tissue from the fibula. Amputation was made necessary not by the type of tumor, but by the local invasiveness and destruction by this "benign" tumor.

Giant cell tumors of bone are rare lesions in a general hospital. We have had 11 examples of this tumor in the past 16 years. The most common locations were in the distal femur, proximal tibia, and distal radius. These three locations constitute about 60% to 70% of all giant cell tumors. While the tumors are most often seen in a long bone, they may rarely be found in other bones, and even in the jaw bones. Though all our cases of giant cell tumor have been in males, according to the literature (Dahlin et al., 1956; Hutter et al., 1962) there is a preponderance in the female sex.

Most of us divide the tumor into three grades. About half the cases are Grade I lesions and following conservative treatment the patients have no further difficulty. Grade II lesions constitute about one-third of the cases and are more aggressive. They are apt to recur and may ultimately become frankly malignant and metastasize. Only about 10% of the cases are frankly sarcomatous from the beginning and diagnosed as Grade III tumors. They must be dealt with by radical measures since metastasis to the lung is a real threat.

The grading of tumors is readily accomplished microscopically in most instances. Grade I lesions show closely packed giant cells containing many nuclei (up to 50!) and few stromal cells. In Grade II tumors the giant cells are less frequent and with fewer nuclei. The stromal cells are abundant, plump, with occasional mitosis. Grade III tumors are obviously sarcomatous with only scattered giant cells. The tumor cells are spindly, anaplastic and with frequent mitotic activity.

Dr. Fairfield Goodale (chairman, department of pathology, MCV): What do you consider is the relationship of this process to the so-called giant cell reparative granulomas seen fairly commonly in the jaw?

Dr. Kay: Some authors (Waldron and Shafer, 1966) consider this lesion similar to the giant cell tumor of long bones. In fact, the only difference from the clinical standpoint is that the jaw lesions occur in a younger age group. This difference may be accounted for by the fact that jaw conditions are apt to be clinically evident at an earlier stage than the long bone lesions which are generally hidden from view. The latter, therefore, are diagnosed relatively late in their course.

Pathological Diagnosis

Giant cell tumor (Grade II) of right fibula, with extension to tibia.

Addendum: Ten months after the operation, there is no evidence of recurrence of the tumor. The patient is making good progress in accommodating to his prosthetic leg.

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