Benign Giant Cell Tumor of Bone

Abstracted from the Bone and Soft Tissue Tumor Course, Mayo Clinic, Rochester, Minnesota, April 17 and 18, 1980.

A team approach is required for the evaluation and management of bone and soft tissue sarcomas, including benign giant cell tumor of bone, which was the diagnosis of this patient's disorder.

Dr. Jeffrey J. Eckardt: A 29-year-old woman was seen in our clinic because of a six-month history of vague shoulder pain. Two weeks before evaluation at our clinic the pain increased acutely, and she was unable to move her shoulder. There was no history of associated trauma, and the patient's general health had been good. Plain roentgenograms revealed a permeative lesion of the proximal humerus extending to the articular surface, with a pathologic fracture at the surgical neck (Fig. 1, left). General examination was unremarkable, except for pain and some swelling about the shoulder and a reluctance to move the extremity because of pain. Other than an erythrocyte sedimentation rate elevated to 44 mm/hr, the results of laboratory tests were normal. A bone scan using $^{99m}$Tc revealed increased uptake only in the region of the lesion. A computed tomographic (CT) scan revealed not only the pathologic fracture but also a small soft tissue component to the lesion (Fig. 1, right).

Dr. Cooper, from this roentgenographic presentation, can you help with the diagnosis?

Dr. Kay L. Cooper: The permeative nature of this
lesion is worrisome. Although the patient’s age and the lesion’s subarticular location are consistent with a giant cell tumor, one also must consider malignant lesions, such as a telangiectatic osteosarcoma, fibrosarcoma, or even metastatic disease. A biopsy specimen would be helpful in this case.

Dr. Eckardt: The indeterminate roentgenographic nature of this lesion makes it important that a biopsy specimen be taken. We almost always use an open biopsy technique, because it obviates tissue sampling errors inherent in needle biopsy. Through a deltopectoral incision, we would biopsy the soft tissue extension of this tumor. If the lesion were an osteosarcoma or fibrosarcoma, we would close the biopsy incision and do an interscapulothoracic amputation, with a wide margin around the biopsy site. However, if the lesion were a benign giant cell tumor, we would close the limited biopsy incision and ellipse it, using an extended deltopectoral incision for the definitive resection. If the pathologist were confident of the findings on frozen section analysis of the biopsy specimen, we would proceed right away with a definitive procedure. However, if there were a doubt, we would close the biopsy site and await the study of permanent sections before doing a definitive procedure.

Dr. Krishnan K. Unni: I am satisfied that the frozen sections in this case show pathology typical of benign giant cell tumor. There are many benign giant cells containing 20 to 30 nuclei scattered uniformly throughout the field.

Dr. Eckardt: Based on Dr. Unni’s interpretation of the frozen section we closed the biopsy site, which we ellipsed, and proceeded immediately with a proximal humerus resection. We performed a hemiarthroplasty with a ceramic prosthesis (Fig. 2). After the operation, the shoulder was placed in an immobilizer for two weeks in order to allow the soft tissue to heal. This was followed by active and passive range-of-motion exercises. At 11 months postoperatively the patient was free of pain and had good passive range of motion of the shoulder. Although elbow, wrist, and hand functions were normal, active motion of the shoulder was limited to 45° of forward flexion and 40° of abduction. This emphasizes some of the functional limitations that can be expected with proximal resection of the humerus.

The roentgenographic classification of giant cell tumors of Campanacci and associates¹ has proved helpful in planning our operations. The rare grade 1 giant cell tumors are totally intraosseous and apparently quiescent. Grade 2 lesions appear to be more active roentgenographically, with thinning of the cortex and ballooning of the intact periosteum. Both grades of lesions are amenable to curettage, cautery, and grafting. A grade 3 tumor has the roentgenographic appearance of aggressiveness, with soft tissue invasion with or without pathologic fracture. The case discussed here illustrates a grade 3 roentgenographic lesion, and the best treatment is resection.

Dr. Cooper, will you give a more detailed discussion of the roentgenographic characteristics of giant cell tumors?

Dr. Cooper: When a giant cell tumor is located at the end of a long bone, the roentgenographic diagnosis is relatively easy. These tumors tend to be purely lytic and eccentrically located, extending to involve the subarticular portion of the bone. Giant cell tumors may be fairly well margined, or they may fade more

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gradually into the adjacent normal bone. Generally there is no rim of sclerosis around the giant cell tumor and, if a rim is visible, a different diagnosis should be considered. This lack of reactive bone formation also occurs in the periosteum. Periosteal new bone in a giant cell tumor is extremely rare in the absence of pathologic fracture. Large lesions may lose their eccentricity within the bone and grow to involve most of the diameter and extend into the metaphyseal area. Occasionally trabeculations can be seen; these represent residual ridges of cortex within the bone. Giant cell tumors may expand the cortex and may destroy it, extending into the soft tissue. Pathologic fractures are not uncommon in aggressive-appearing lesions. The permeative nature of giant cell tumors was illustrated in the case presented. In such situations malignant alternative diagnoses must be considered, and the roentgenographic appearance is not classic. In tumors of the ilium and sacrum, the diagnosis may be more difficult. Giant cell tumors tend to be subarticular in relation to the sacroiliac joint. Giant cell tumors in the spinal column are uncommon above the sacrum; when they do occur in the vertebral column they tend to be centered in the vertebral body, appearing as purely lytic lesions, and may expand the bone. This is in contrast with aneurysmal bone cysts and osteoblastomas—lesions that are found more frequently in the posterior elements.

Postoperatively, when giant cell tumors that have been grafted are evaluated, a recurrence is identified as an area of lucency at the graft site or of resorption of the bone grafts. Calcified deposits may be present within soft tissue recurrences of giant cell tumors.

**Dr. Eckardt:** Dr. Unni, will you discuss giant cell tumors from the pathologist’s point of view?

**Dr. Unni:** The permanent sections from this case are very typical of benign giant cell tumor (Fig. 3). There are many benign giant cells scattered more or less uniformly about the field, each containing 20 to 30 nuclei. The nuclei of giant cells have the same appearance as nuclei of the mononuclear cells in the background. The nuclei in a typical giant cell tumor are round or oval and are not spindly. Mitotic activity in the stromal cells of benign giant cell tumors is common. If there are no mitotic figures the lesion may be of another type, because mitotic figures are so common in benign giant cell tumor of bone. The giant cell tumor in the patient we are discussing has areas that have undergone infarction. In most bone tumors, if areas of necrosis are visible, one is concerned that the lesion is malignant. This is one instance in which infarction does not suggest malignancy. Necrosis is found frequently in giant cell tumors if one looks for it.

Occasionally there is vascular invasion by benign giant cell tumor, and the typical giant cell tumor cells within the vessels are near the lesion. Probably this is not significant, because metastatic disease is rare. However, several cases have been reported in which benign giant cell tumor metastasized to the lungs. Although no patient has died of this condition, one patient in our experience has hundreds of small lesions in both lungs. In the lung, these metastatic lesions are seen histologically as a typical benign giant cell tumor that produces bone around the periphery, as there would be in a soft tissue recurrence.

As with other benign lesions, when giant cell tumors extend into the soft tissue, they push the soft tissue rather than invade it, and usually a shell of ossification completely surrounds the soft tissue extension. Typically soft tissue recurrences, when
seen histologically, are completely enveloped in shells of ossification.

Examination of a gross specimen after resection shows a tendency for the tumor to permeate the interstices of the cortex, and this permeation probably accounts for the fact that curettage alone results in a high incidence of local recurrence. The gross specimen of the giant cell tumor may appear to be very cystic and have the appearance of an aneurysmal bone cyst; aneurysmal bone cystlike areas may even be seen on histologic section.

We do not grade benign giant cell tumors histologically because we have not found any reliable grading system, nor has grading been helpful in predicting tumor behavior.

To be classified as a malignant giant cell tumor, the lesion must have areas of typical benign giant cell tumor mixed with areas of fibrosarcoma or osteosarcoma, or a fibrosarcoma or an osteosarcoma must be present at the site of a previously documented benign giant cell tumor that was treated with or without radiation. The presence of osteoclastlike giant cells in a malignant-appearing stroma is not adequate for the diagnosis of a malignant giant cell tumor. This definition, although arbitrary, has worked very well for us in relation to the clinical course of giant cell tumors.

Dr. Eckardt: Our series of giant cell tumors covers 266 tumors in 264 patients. This points out the rare multifocal potential of benign giant cell tumors. There is a definite predominance in females, and 85% of the patients were more than 20 years of age at diagnosis. Giant cell tumors are found most frequently about the knee; in our series, 72 were in the distal femur and 56 were in the proximal tibia. The third most frequent site was the distal radius, followed by the sacrum and the axial skeleton.

Included in our series of 264 patients are 20 patients with malignant giant cell tumor. Thirteen of these 20 developed malignant giant cell tumors after irradiation of benign giant cell tumors. Of the other seven patients, five had areas of sarcoma mixed with areas of benign giant cell tumor at the first operation, and two developed sarcomas at sites of previously curetted benign giant cell tumors. This suggests that the giant cell tumor generally is a benign entity and should be treated as such, both initially and in recurrences. The malignancy rate of 2.6% in our series is similar to that of 1.9% recently reported.

The preoperative evaluation of giant cell tumors should include routine medical evaluation to rule out such conditions as the brown tumor of hyperparathyroidism and metastatic disease. In addition to routine roentgenograms, arteriograms have been helpful for evaluation of these lesions about the knee. More recently, we have utilized CT scanning in this area as well as in the pelvis and sacrum. Open biopsy is a critical aspect of the management of these conditions.

Treatment choices for giant cell tumors are numerous. In expendable areas, such as the fibula, distal ulna, and ribs, total en bloc resection is the treatment of choice and uniformly leads to a good result. However, most giant cell tumors do not occur in these areas and various techniques, including curettage and grafting, resection and arthrodesis, resection and reconstruction, and amputation and radiation therapy, should be considered. When the roentgenographic appearance of the giant cell tumor is that of grade 1 or 2 on the Campanacci scale, and the tumor is in an accessible location, such as the end of a long bone, our initial preference for treatment is curettage, chemical cautery, and grafting. Chemical cautery with phenol is preferred, although thermal cautery with liquid nitrogen has been advocated by others. Critical to effective curettage and grafting is complete exteriorization of the lesion (Fig. 4). Attempts at curettage through a small hole in the cortex routinely lead to recurrence because some of the tumor is left behind. After wide exteriorization and vigorous curettage, the soft tissues are packed off...
with Vaseline gauze and moistened sponges, as seen in the proximal tibial lesion shown in Fig. 5, left. The curetted tumor cavity is then filled with phenol for 30-45 seconds (Fig. 5, right). Phenol, which coagulates protein, is effective in reaching the interstices of the cortical bone into which the giant cell tumor has permeated. The phenol is removed with sponges, and the cavity is rinsed with 95% ethyl alcohol. The curetted cavity is then lavaged vigorously with large amounts of isotonic saline. After curettage and chemical cautery, autogenous bone grafts are placed. A tourniquet is used when practical.

Giant cell tumors not only can recur in bone and soft tissue, but also can be transplanted to the bone graft donor site. Therefore, all bone grafts should be taken with a complete second surgical setup, including separate gloves, new instruments, and possibly re-prepping and draping the patient if there is a question of cross-contamination.

In our series, local recurrence for benign giant cell tumor was about 50% overall. Our series included the difficult-to-manage lesions in the axial skeleton. For lesions of the extremity, our overall recurrence rate
was only 25% using the method described previously. No significant complications were noted with the cautery technique, and there have been no pathologic fractures, vascular problems, or need for prolonged casting or bracing.

For giant cell tumors of the distal radius, curettage and grafting, arthrodese, or fibular autograft replacement may be considered the primary procedure. It is remarkable how well the proximal fibula simulates the contour of the distal radius.

Radiation therapy is reserved for the management of giant cell tumors that are inaccessible by surgery, such as those of the pelvis and axial skeleton. Although we have had excellent results with radiation therapy in these situations, the problem of postradiation sarcoma is real and is an unpredictable sequela of this form of treatment.

Pain or swelling or a decrease in range of motion over an area in which a giant cell tumor has been treated suggests a recurrence. Most recurrences appear within two years of primary treatment. Generally, the management of a recurrence should be repeat curettage, cautery, and grafting, if possible. However, the presence of a large soft tissue extension, pathologic fracture, or fracture into a joint indicates the need for arthrodese or resection. For primary or recurrent aggressive lesions about the knee, a special custom prosthesis such as the Walldius total knee replacement may be used in selected patients. Cadaver allografts for such lesions also have been used, and various arthrodese techniques also are available. These would include Enneking's "turn-up, turn-down" technique or a technique of contra]lateral femoral shortening (Fig. 6). Because of the tendency for recurrence, followup at frequent intervals is recommended.

In summary, although amputation and en bloc resection provide a uniform cure for giant cell tumor, amputation is rarely necessary. En bloc resection requires the use of custom joint replacement and allograft or arthrodese techniques. However, because the functional results after curettage, chemical cautery, and grafting are clearly superior to those after replacement and arthrodese techniques, the former approach is the preferred primary treatment for most giant cell tumors of bone.

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