Periosteal Osteosarcoma

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An analysis of 6 patients with periosteal osteosarcoma treated by the authors along with a review of 55 patients reported in the literature demonstrates that periosteal osteosarcoma is distinctly different from conventional osteosarcoma or periosteal chondrosarcoma. Periosteal osteosarcoma is a less aggressive tumor than conventional osteosarcoma. It is a relatively well-differentiated chondroblastic osteosarcoma occurring on the surface of the long bones of the extremities. Three patients demonstrated frank medullary invasion of tumor, two grossly and one microsurgically. Patients treated with marginal resection had a 70% local recurrence rate. Patients receiving wide resection or primary amputation have survived longer with less recurrence of disease. Overall, 10 of 61 patients are dead with metastatic disease with a mean reported follow-up of 6 years and 7 months. Adjunctive therapy has been of no demonstrable aid in terms of prolonging survival. Medullary extension of this tumor should not be used to exclude this diagnosis. The authors believe that the treatment of choice is wide resection without adjunctive chemotherapy.

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PERIOSTEAL OSTEOSARCOMA was described by Lichtenstein in 1959[1] as the periosteal counterpart of central or intramedullary osteosarcoma. Periosteal osteosarcoma was described as a distinct clinicopathologic entity by Unni and colleagues[2] in 1976 and has been supported by other authors[3,4] as being distinctly different from conventional osteogenic sarcoma. Although in the description of periosteal osteosarcoma offered by Unni and co-workers, intramedullary involvement is used as a means to exclude the diagnosis, we suggest that an area of medullary tumor extention should not be used to exclude the diagnosis of periosteal osteosarcoma. The radiographic, histologic, and biologic nature of this tumor is distinct enough to allow the diagnosis in the face of medullary extention. The recognition of this tumor allows the treating physician to spare these patients the radical and dangerous treatment that is warranted for conventional osteosarcoma. Sixty-one patients with periosteal osteosarcoma, including six treated by the authors, have been reviewed and are reported in this article.

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Case Reports

Case 1

A 16-year-old black girl presented with a 2-month history of vague, aching pains over her right medial proximal tibia with findings of a firm, indurated mass at this site. Roentgenograms demonstrated an exophytic lesion, 7 × 1 cm, with calcific density, zones of lucency, and moderate reactive margination (Fig. 1). A bone scan revealed only increased uptake in the proximal tibia; there was no evidence of metastases. An incisional biopsy of the right medial and proximal tibia was performed, and a glistening white tumor was found with soft tissue extension along the medial collateral ligament. On frozen section microscopy, malignant cartilaginous tissue was seen; the wound was then closed. A diagnosis of periosteal osteosarcoma was made by permanent section studies (Figs. 2–4). Ten days later an above-knee amputation was done. Microscopic study of the specimen revealed a small focus of intramedullary extension of the tumor. The patient received multidrug adjuvant chemotherapy consisting of 15 g of methotrexate each week for 8 weeks, then switched to 3 weeks. Vincristine, 2 mg, was given 2 hours before methotrexate administration. Chemotherapy was continued for 1 year. The patient has been followed for 60 months without evidence of recurrence of disease.

Case 2

A 40-year-old black man presented with swelling along his right proximal tibia that had been present for 2 months and a

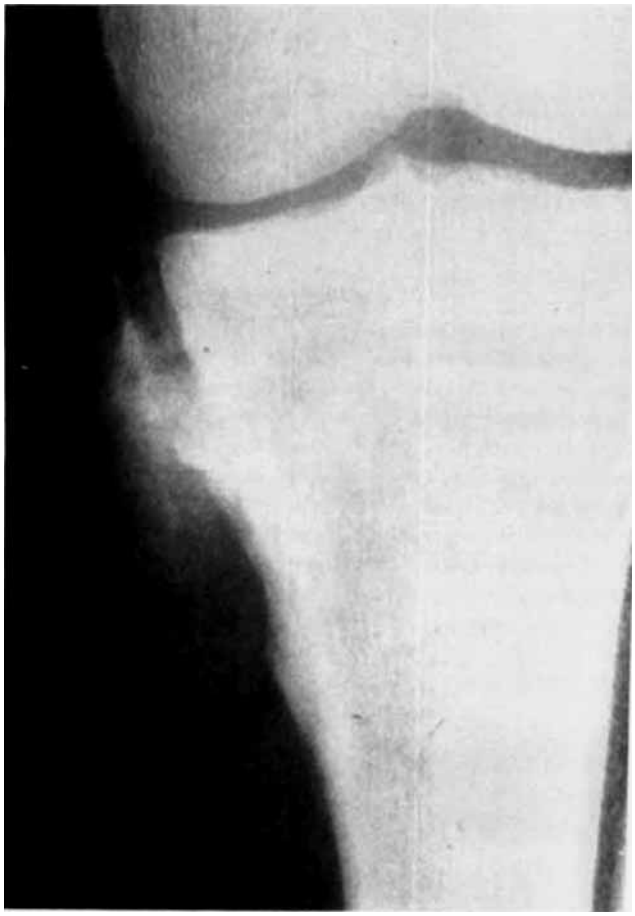


FIG. 1. Preoperative roentgenogram of Case 1. This lesion of the right proximal tibia has its center on the periosteal surface. It has an ill-defined, partially mineralized soft tissue mass.

palpable, immobile, nontender mass 4.5 × 7 cm in size was noted. Roentgenograms revealed an exophytic proximal right tibial lesion 7 × 3 cm, of calcific density with zones of lucency, without radiographic evidence of medullary involvement (Fig. 5A). A computerized tomography (CT) scan of the tibia demonstrated no marrow involvement, and a chest roentgenogram was within normal limits. A bone scan showed increased uptake at this site. An incisional biopsy was performed on October 24, 1979 with frozen section findings of malignant osteoid-producing tumor. A wide resection was then performed, followed by arthrodesis of the knee over a custom Sampson rod with autogenous bone graft. The gross specimen demonstrated cortical invasion and medullary extension of the tumor (Fig. 5B). The patient did not receive adjuvant chemotherapy. At 39 months follow-up, he is without evidence of local or metastatic recurrence (Fig. 5C).

Case 3

A 21-year-old black man presented with a history of pain in his left distal anterolateral femur. Roentgenograms of this area revealed a sessile cortical lesion, 5.5 × 1 cm, of calcific density with zones of lucency, no reactive margination, and no soft tissue involvement. A chest roentgenogram was within normal limits. An incisional biopsy was done in March 1980 and revealed a predominantly chondroblastic osteoid-producing tumor. The diagnosis of periosteal osteosarcoma was made at the Armed Forces Institute of Pathology. A wide resection was performed in May 1980. There was no medullary involvement by the tumor. He did not require a definitive reconstructive procedure. The patient returned in January 1981 with complaints of pain in his surgical site with associated redness and swelling. Repeat chest roentgenogram was normal, and a bone scan revealed slightly increased uptake in the affected area. An incisional biopsy was then performed and demonstrated no local recurrence. At 24 months follow-up, he has no evidence of local or metastatic recurrence.

Case 4

A 15-year-old white girl was referred with a 3-week history of painful cramping and swelling of her left leg. Physical examination revealed a firm mass along the left proximal fibula. Roentgenogram revealed an exophytic mass, 8 × 3.5 cm, with flocculent calcific densities peripherally and calcific densities and zones of lucency centrally (Fig. 6A). A CT scan

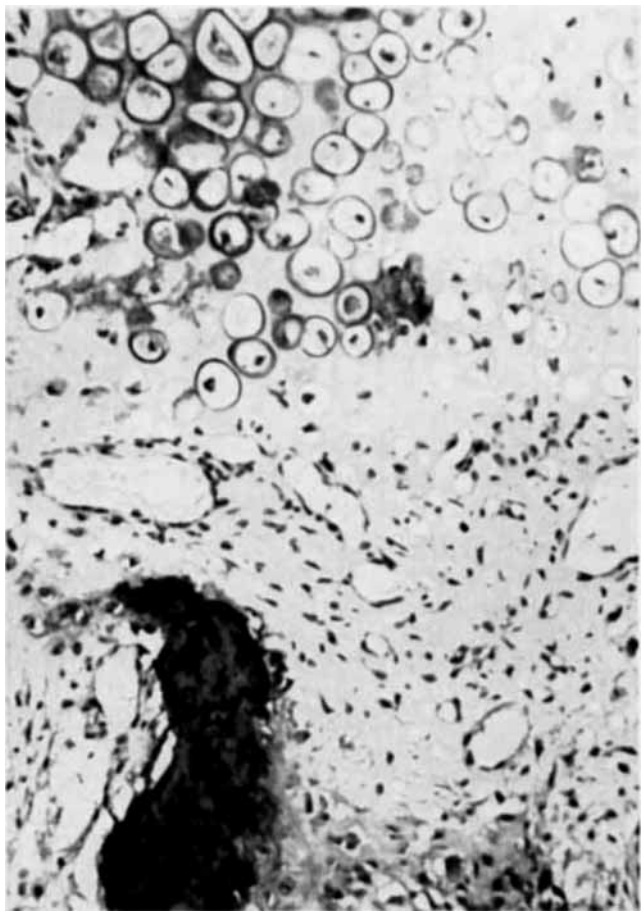


FIG. 2. Photomicrograph of a periosteal osteosarcoma showing a lobule of malignant cartilage at the top and a spicule of tumor bone with adjacent tumor osteoid below (H & E, original magnification ×120).

of the left fibula revealed a soft tissue mass around the bone, extending along the interosseous membrane, with questionable medullary involvement. A bone scan showed only increased uptake in the left fibula. Her chest roentgenogram and chest CT scans were normal. Incisional biopsy on June 9, 1982 showed a chondroblastic, osteoid-producing malignant lesion located outside of the cortex. On August 11, 1982 the patient had an attemped wide resection of the left fibula. Gross cortical invasion with medullary extension of the tumor was evident on hemisection of the surgical specimen (Fig. 6B). Permanent sections revealed a marginal resection with areas of high-grade osteosarcoma. We believe that a marginal excision for a high-grade sarcoma is at high risk for local recurrence.[5] For this reason, treatment was supplemented with 100 mg of Adriamycin (doxorubicin) over 80 hours by continuous infusion of the left superficial femoral artery, followed by radiation therapy of 3000 rad in 10 fractions to the left proximal fibular area.[6,7] After 14 months of follow-up, she is without recurrence (Fig. 6C).

Case 5

A 28-year-old white man had pain in the lateral aspect of his right tibia, exacerbated by activity for 2 months. When he was first seen, he was found to have a firm, nontender bony mass along the posterior medial aspect of the proximal right tibia. Chest roentgenogram was within normal limits. Incisional biopsy was performed on December 4, 1978, and a diagnosis of parosteal osteosarcoma was made. Three days later a marginal excision was performed. A local recurrence was found 11 months later, and this was treated with an above-knee amputation. The patient was fitted with a prosthesis and remained free of known disease for 2 years and 6 months, until a palpable mass was found along the superior pubic rami on the right side. A needle biopsy specimen of this mass revealed chrondroblastic osteosarcoma. A review of all the patient's roentgenograms and pathologic material confirmed a diagnosis of periosteal osteosarcoma. The patient then received 100 mg of Adriamycin over an 80-hour period though his right femoral artery, then 1750 rad of radiation to his right groin over 10 days. A CT scan of the lungs and a chest roentgenogram showed no metastases. A resection of the right groin mass was then performed, with findings of tumor thrombus in the right femoral and iliac veins with extension into the inferior vena cava and soft tissue of the left side of the

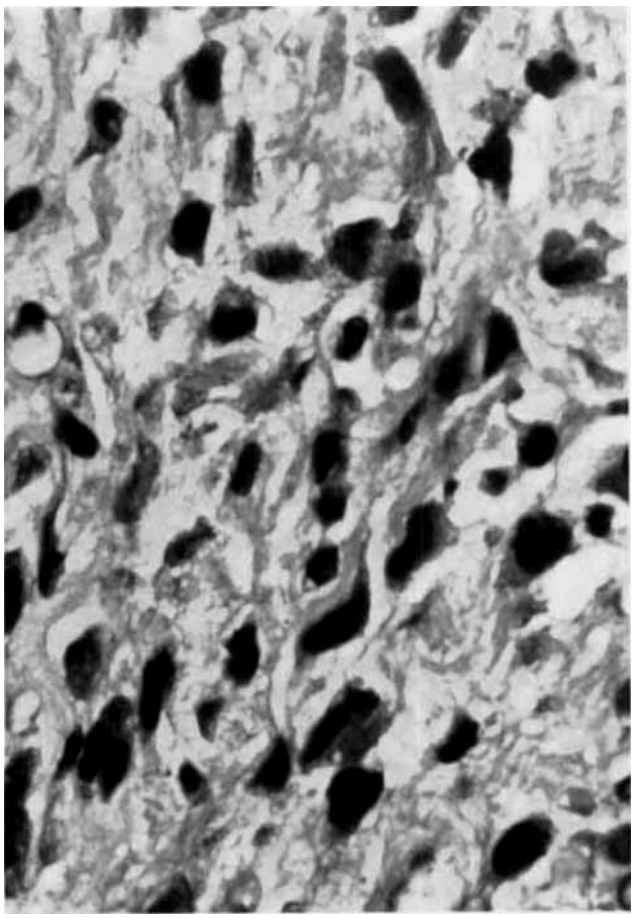


FIG. 3. Photomicrograph demonstrating the malignant spindle cells producing osteoid found within the primarily cartilaginous tissue in periosteal osteosarcoma (H & E, original magnification ×480).

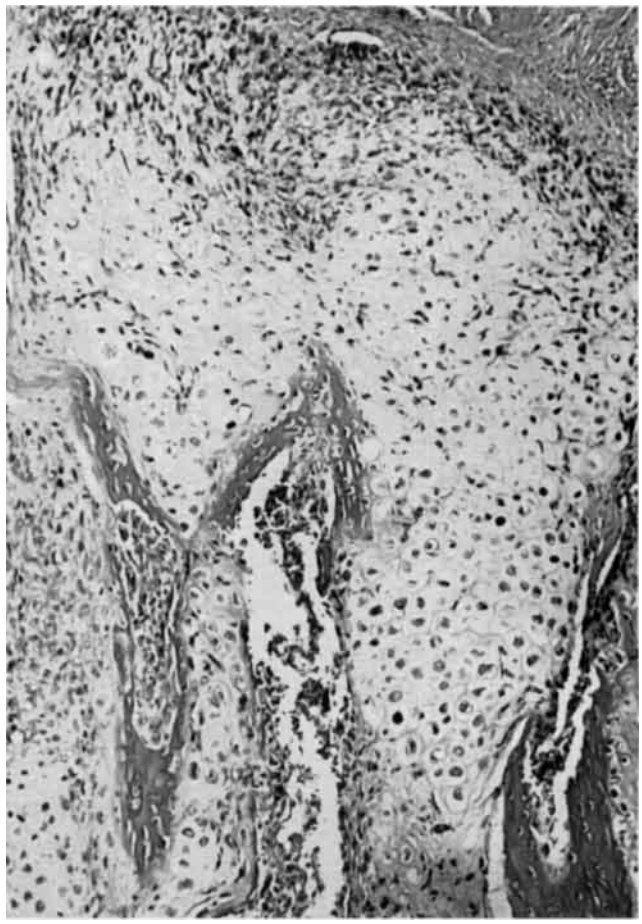
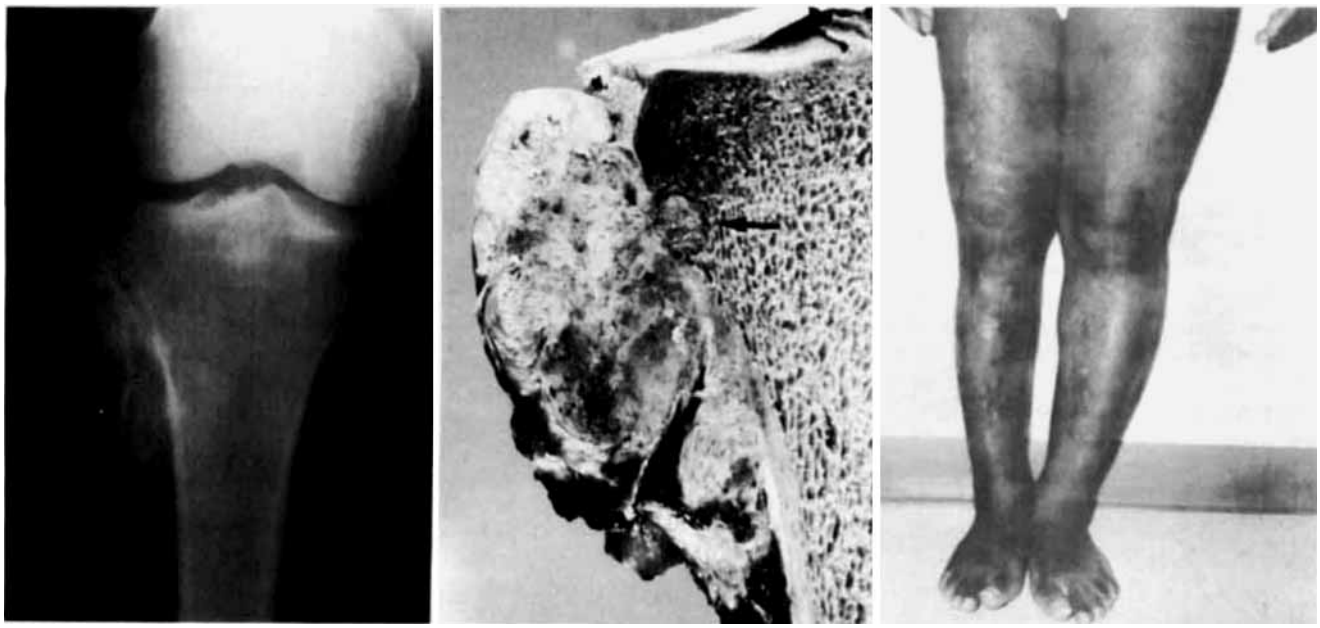
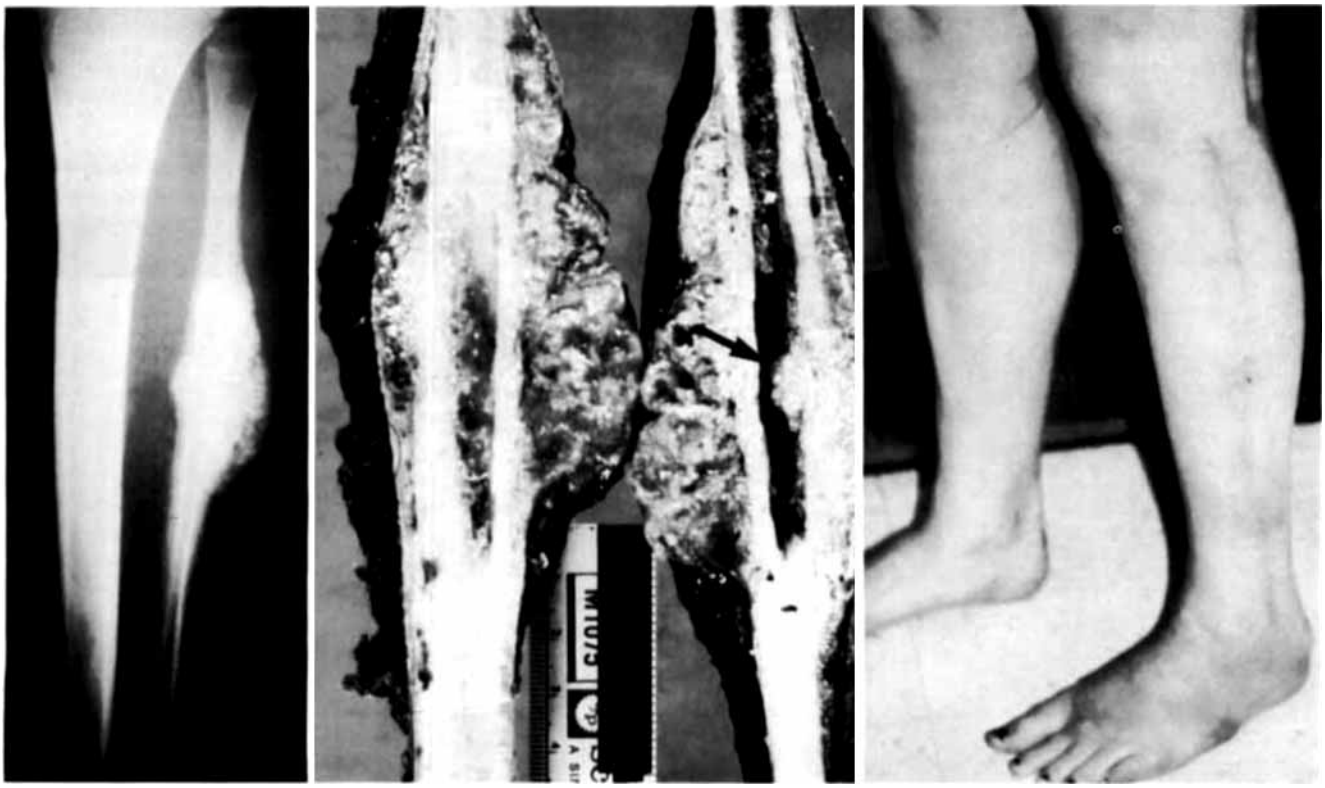


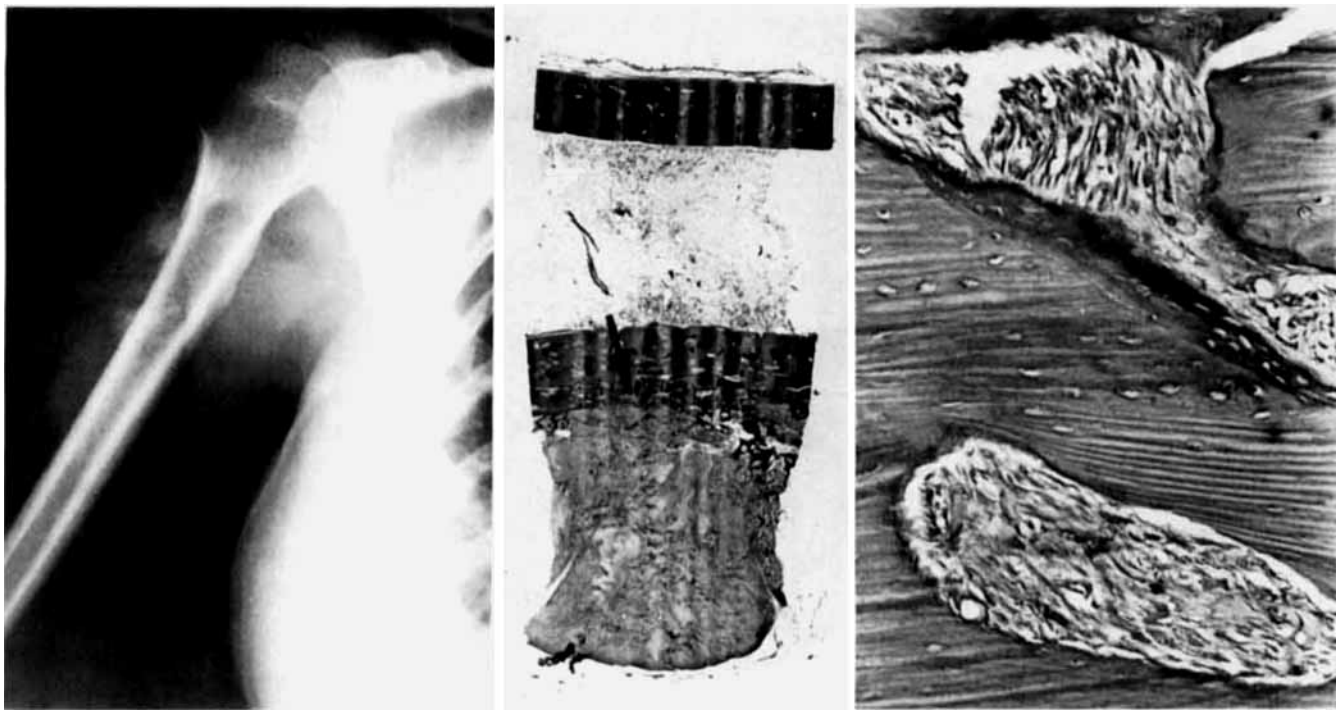
FIG. 4. Photomicrograph showing the typical lobule of malignant cartilage, which is the dominant component in periosteal osteosarcoma. Enchondral ossification, which is seen centrally, accounts for some of the radiodensity seen on roentgenograms (H & E, original magnification ×120).



FIGS. 5A–5C. (A, left) Roentgenogram of right tibia (Case 2) shows a periosteal lesion with a more well-defined soft tissue mass. No medullary involvement was suspected preoperatively. (B, center) Hemisected gross specimen (Case 2) demonstrates cortical and medullary bone penetration by the tumor. Black arrow indicates the area of medullary extension. (C, right) Photograph of the patient (Case 2) shows him bearing weight on the affected extremity 39 months after resection arthrodesis of the knee.



FIGS. 6A–6C. (A, left) Roentgenogram of left fibula (Case 4) demonstrates a periosteal lesion encircling the fibula. The flocculent calcification is very suggestive of cartilaginous tissue. Medullary involvement was suspected from tomograms made of the lesion. (B, center) Hemisected gross specimen (Case 4) demonstrates a discrete of focus of extension of the tumor into the medullary canal of the fibula (indicated by black arrow). (C, right) Photograph of the patient (Case 4) shows her bearing weight on the affected extremity 14 months after en bloc resection of the fibula. She was not given systemic chemotherapy.



FIGS. 7A–7C. (A, left) Roentgenogram of right proximal humerus (Case 6) demonstrates saucerization of the lateral cortex and the periosteal reaction of a Codman's triangle. (B, center) A photomicrograph of a longitudinal section of the humerus (Case 6) shows the periosteal osteosarcoma thinning the underlying cortex and invading the cortex (black arrow) but not the medullary bone (H & E, original magnification ×1). (C, right) Photomicrograph of the cortical bone underlying the tumor in Case 6 shows islands of sarcoma permeating dense cortical bone (H & E, original magnification ×120).

pelvis. An inferior venacavagram was performed, demonstrating extension of the tumor to the level of the renal veins and into the left common iliac vein. A resection of the inferior vena cava to a point just distal to the left renal vein and to the left common iliac vein was performed, but grossly unresectable tumor was left in the right hemipelvis. The patient received 450 mg/m^2 of systemic Adriamycin chemotherapy. He was followed up for 4 years and 9 months from diagnosis, until he died of abdominal extension without evidence of pulmonary metastases.

Case 6

A 32-year-old right-hand-dominant woman with a 5-month history of intermittent pain in the right shoulder noticed a mass 2 months prior to admission. Physical examination revealed a firm, nontender soft tissue mass measuring 8 × 4 cm under the deltoid and fixed to the lateral proximal humerus. Roentgenograms showed a 6-cm bone-forming lesion of the lateral proximally and distally, with thinning of the underlying cortex but no medullary involvement (Fig. 7A). Bone scan showed marked activity increase eccentrically, corresponding to the plain radiograph with only a slight increase in intramedullary activity. A CT scan of the shoulder showed a bone-forming tumor rising from the lateral humeral cortex with no evidence of penetration. The patient underwent a Craig needle biopsy with a frozen section diagnosis of malignant chondroblastic tumor, consistent with periosteal or juxtacortical osteosarcoma. Permanent sections revealed chondroblastic tissue invading underlying cortex (Figs. 7B and 7C). The patient underwent an en bloc resection of the proximal 19 cm of the humerus, deltoid, and adjacent soft tissue, with preservation of the musculocutaneous and radial nerves. Intraoperatively, the margins of resection were found to be free of reactive tissue or tumor. Reconstruction of the defect was accomplished by a custom designed 190-mm prosthetic humeral head fixed with bone cement into the distal humerus. The prosthesis was suspended by Mercelene tape through drill holes in the scapula and clavicle. Postoperatively the patient has no active shoulder abduction, but shoulder strength and stability are good. The patient has no evidence of local recurrence or metastatic disease at 16 months follow-up.

Discussion

As suggested by its name, periosteal osteosarcoma is an osteoid-producing sarcoma apparently arising in the periosteum of bone. Unni and co-workers described a sarcoma of chrondroblastic nature that produced osteoid and that was located on the cortex of long bones of the lower extremity and had no frank medullary involvement.[2] These 11 tumors were selected from more than 5,000 primary bone tumors at the Mayo Clinic. Spjut and associates[4] and Bertoni and others[3] have reported their experience with periosteal osteosarcoma.

The 61 patients now reported with periosteal osteosarcoma range in age from 9 to 62 years, with 32 male

and 29 female patients. There was no peak decade of incidence. Twenty-eight tumors were located in the tibia, 25 in the femur, 5 in the humerus, 3 in the fibula, and one in the ilium (98% in the long bones of the extremities). Symptoms were pain and swelling of the affected extremity, usually of short duration (less than 3 months). The average tumor size was 7 × 1.7 cm.

The radiographic presentation of periosteal osteosarcoma is suggestive of the diagnosis but not unique or diagnostic. The lesion typically occurs on the periosteal surface of the medial or lateral metaphyseal portion of the long bones of the extremities. The proximal tibia is the favored location (Figs. 1 and 5A).

The cortical bone underlying the tumor appears intact, but it may be thickened by reaction to the lesion or thinned by the tumor itself (Figs. 6A and 7A). The layered periosteal reaction of a Codman's triangle is frequently seen at the superior or inferior limits of the tumor (Fig. 7A).

The epicenter of the tumor itself is on the periosteal surface of the bone. The soft tissue extent of the tumor, although generally lucent, is of greater density than the surrounding soft tissue and can usually be delineated. The tumor mass has within it scattered areas of calcific density, both the stippled calcification of areas of calcified cartilage and the fine striations of tumor bone (Figs. 1, 5A, 6A, and 7A). The sunburst appearance of radiating spicules of mineralized tumor osteoid at right angles to the cortical bone is frequently seen.

The microscopic appearance of the periosteal osteosarcomas that form the basis of this report are considered to be sufficiently characteristic to distinguish this lesion (Figs. 2, 3, and 4). In each of the lesions studied, cartilage constituted a prominent feature and was present as well-defined lobules, some of which were confluent. The cellular features were those of malignant cartilage, usually with a low order of malignancy. Many of these lobules showed areas of endochrondral ossification, particularly in their central portions. The peripheral portions of some of the lobules were rimmed by malignant spindle cells. Scattered throughout the lesion were areas composed of delicate, lacy seams of osteoid associated with entrapped malignant osteoblasts.

Areas of fibroblastic differentiation with mature bone, characteristic of parosteal osteosarcoma, were not present.

The typical intramedullary osteosarcoma is characterized by the presence of delicate seams of osteoid associated with cells showing the cytologic features of a malignant neoplasm. This is not the dominant feature in periosteal osteosarcoma.

In contrast to periosteal osteosarcoma, periosteal chondrosarcoma is characterized by lobules of fairly well differentiated hyaline cartilage. Myxoid areas occur only infrequently.[3] The cellularity noted at the periphery of the lobules of cartilage in periosteal osteosarcoma is not a feature in periosteal chondrosarcoma. Tumor osteoid is not present.

Treatment of the 61 patients varied in spectrum from marginal resection to amputation, with or without adjuvant radiation and chemotherapy. Twenty-one patients originally had marginal resection, with 15 having local recurrences (70%). Eight of these have required amputation, and six had more extensive local resections. Five of 21 have died of metastatic disease from 9 months to 7 years after presentation. One of these five had received adjuvant chemotherapy, and two of these five had received radiation.

Twenty-five patients had amputation as their primary procedure, with four patients later dying with metastatic disease. Six of these 25 patients received chemotherapy, and 2 of 25 received radiation.

Overall, 10 of 61 patients have died with metastatic disease, with a mean reported follow-up of 6 years and 7 months.

Plea for Acceptance of Medullary Involvement

Unni and associates have stated that they accept no medullary involvement in their classification of periosteal osteosarcomas. Spjut and colleagues noted microscopic medullary involvement in one case.[4] We have observed gross medullary extension of this tumor in two cases (Cases 2 and 4), microscopic medullary extension in an additional case (Case 1), and cortical extension in another (Case 6). Medullary extension does not seem to change the biologic aggressiveness of the tumor or to herald a poor prognosis.

It is accepted that the natural history of this chondroblastic osteosarcoma arising on the surface of bone is different from that of conventional osteosarcoma. We speculate the less aggressive nature of this tumor might be explained by the location of the cells of origin. These tumors appear to arise from the undifferentiated cells of the periosteal sheath. Sarcomatous transformation yields primarily chondroblastic tissue distinguishable from high-grade osteosarcoma arising on the surface of bone that is primarily osteoblastic.[8]

We believe that the natural course of periosteal osteosarcoma is for the neoplasm to grow relatively slowly on the surface of the bone. The margin of the tumor with surrounding tissue has a pushing nature like a chrondrosarcoma, rather than an infiltrating margin like a conventional osteosarcoma. The underlying cortical bone acts as a barrier for some time as the tumor slowly penetrates (Figs. 7B and 7C). Depending on the nature of the individual tumor, the ability of the host bone to respond, and the time before treatment, the periosteal osteosarcoma may or may not penetrate the underlying

medullary bone. The tumor's pushing border makes it easier to treat surgically, requiring removal of less normal tissue at the periphery to remove every tumor cell. This idea is reinforced by the 13% local recurrence rate with wide resections reported for periosteal osteosarcomas.

The periosteal osteosarcoma metastasizes later and less frequently than conventional osteosarcoma arising in the rich, vascular sinusoids of the metaphyseal bone. The cases now reported suggest a metastatic rate of 15% to 20%[2,3] with adequate treatment (no local recurrence) of the primary tumor. Currently, we do not recommend adjuvant chemotherapy because of this lower metastatic potential, the historic unresponsiveness of chondroblastic tissue to chemotherapy, and the state of the art in adjuvant chemotherapy for conventional osteosarcoma.

We are making a plea for the acceptance of intramedullary involvement in periosteal osteosarcoma when a tumor presents radiographically on the surface of a long bone with the epicenter of the tumor being in the periosteum. There should be calcific densities in the mass without the dense, well-differentiated tumor bone of parosteal osteosarcoma. The histologic picture is that of a primary chondroblastic osteosarcoma with a predominance of low-grade malignant cartilage and only scattered areas of lacy tumor osteoid. If these tumors with areas of medullary involvement are treated as periosteal osteosarcomas, limb salvage surgery can at times produce good functional extremities (Figs. 6C and 7C), and the patient can be spared the dangers of very toxic chemotherapy without an unacceptable risk of metastases.

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