CALIFORNIA TUMOR TISSUE REGISTRY

99TH SEMI-ANNUAL CANCER SEMINAR

ON

TUMORS AND TUMOR-LIKE CONDITIONS OF THE BONE

CASE HISTORIES

CO-MODERATORS:

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December 3, 1995
Ritz Carlton Hotel
San Francisco, California

CHAIRMAN:

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Chief, Department of Pathology
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San Francisco, California
Tumors & Tumor-like Conditions of the Bone

CASE #1 - ACCESSION #27813
A 61-year-old man presented with a swelling of the chest wall, present for at least four years. No follow up is available. (Contributed by K. Unni, M.D., Rochester, MN.)

CASE #2 - ACCESSION #27446
A 69-year-old female complained of increasing pain in her left leg. She had undergone mastectomy for breast carcinoma nine months earlier. (Contributed by A. Martinez, M.D., Tustin, CA.)

CASE #3 - ACCESSION #25658
A 69-year-old woman had a six-months' history of aching in the right shoulder. Physical examination revealed a palpable mass. Patient developed multiple bilateral pulmonary metastases 14 months later. (Contributed by D. Kahn, M.D., Sylmar, CA.)

CASE #4 - ACCESSION #27817
A 19-year-old man complained of groin pain for one year. He had lost twenty pounds of weight. Patient underwent preoperative chemotherapy and disarticulation at the hip. He died fourteen months later with widespread metastatic disease. (Contributed by K. Unni, M.D., Rochester, MN.)

CASE #5 - ACCESSION #27815
A 28-year-old woman had pain in the chest wall for 10 months. The lesion was excised in fragments. There was no evidence of disease five years later. (Contributed by K. Unni, M.D., Rochester, MN.)

CASE #6 - ACCESSION #27811
A 14-year-old girl suffered a fracture of her femur while in camp. She was completely asymptomatic until then. Patient underwent disarticulation and chemotherapy. She was doing well at five years. (Contributed by K. Unni, M.D., Rochester, MN.)

CASE #7 - ACCESSION #27806
A 6-year-old girl complained of pain in the leg for one week. The leg was amputated, and a pulmonary and rib metastasis resected. She underwent chemotherapy, and was alive 18 years later without evidence of disease. She is awaiting a heart transplant. (Contributed by K. Unni, M.D., Rochester, MN.)
Tumors & Tumor-like Conditions of the Bone

CASE #8 - ACCESSION #27812

An 11-year-old boy had a painless lump in the lower leg for two months. He was brought by his father, who was dying of lung cancer. Patient underwent an above the knee amputation. He was well seven and a half years later. (Contributed by K. Unni, M.D., Rochester, MN.)

CASE #9 - ACCESSION #27807

A 50-year-old man presented with a fracture through the distal femur. The tumor was resected. Amputation for mechanical reasons was performed at four years, with no evidence of tumor. (Contributed by K. Unni, M.D., Rochester, MN.)

CASE #10 - ACCESSION #27816

A 13-year-old boy presented with swelling of the thigh. He had a lesion in the same site six years previously. Patient underwent amputation and chemotherapy. He was well two years later. (Contributed by K. Unni, M.D., Rochester, MN.)

CASE #11 - ACCESSION #27814

A 54-year-old woman presented with a painful, swollen arm of four years duration. Patient was treated with forequarter amputation, and is believed to have died within months. (Contributed by K. Unni, M.D., Rochester, MN.)

CASE #12 - ACCESSION #27843

A 48-year-old woman, with a previous history of papillary carcinoma of the thyroid, presented with vague leg and back pain. She had been treated with 4000 rads. Patient was treated with internal hemipelvectomy, and required 78 units of blood. She developed an infection and died with systemic infection. (Contributed by K. Unni, M.D., Rochester, MN.)

CASE #13 - ACCESSION #27818

A 79-year-old man presented with pain and swelling of the lower leg for 10 years. Patient was treated with an above the knee amputation. He was well at one year, and driving a car. (Contributed by K. Unni, M.D., Rochester, MN.)
CASE #14 - ACCESSION #26787
An 85-year-old man presented with a 2-3 month history of constipation and perineal and rectal pain. He had pain in the lower back for two years. Physical examination revealed a presacral mass. Recurrence developed two years later. He developed carcinoma of the colon at the same time. Five years later, he had a pelvic mass and mediastinal and supravacular metastases. (Contributed by W. Carroll, M.D., Santa Barbara, CA.)

CASE #15 - ACCESSION #23018
A 30-year-old woman presented with increasing pain in the right knee for six months. She had mild knee pain for four years following an automobile accident. The lesion was curedtted. There is no further follow up available. (Contributed by J. Blanchard, M.D., Santa Barbara, CA.)

CASE #16 - ACCESSION #27810
A 64-year-old woman presented with pain in the hip of short duration. The patient had a thyroideotomy 21 years previously and mediastinal lymph node metastasis 14 years prior. She died 13 months after the hip replacement. (Contributed by K. Unni, M.D., Rochester, MN.)

CASE #17 - ACCESSION #27764
An 8-year-old girl had pain in her left knee for three months. The lesion was curedtted. Three months later, there was no evidence of disease. (Contributed by G. W. Saukel, M.D., Loma Linda, CA.)

CASE #18 - ACCESSION #25801
A 51-year-old woman had a long history of back pain. X-rays of the lumbosacral region showed a lesion in the proximal femur. The patient was well 18 years later. (Contributed by P. Flanagan, M.D., Huntington Beach, CA.)

CASE #19 - ACCESSION #27808
A 13-year-old boy presented with a gradually enlarging, tender swelling of his skull for three years. The lesion was excised. Skeletal survey was negative. The patient was to come back six months later for cranioplasty. (Contributed by K. Unni, M.D., Rochester, MN.)

CASE #20 - ACCESSION #27809
A 30-year-old man presented with the second recurrence of a swelling of his fifth finger. This is a recent case, with no follow up available. (Contributed by K. Unni, M.D., Rochester, MN.)
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TUMOR AND TUMOR-LIKE CONDITIONS OF THE BONE

K. Krishnan Unni, B.S., M.B.
Richard McLeod, M.D.

TABLE OF CONTENTS:

<table>
<thead>
<tr>
<th>CASE #1 - ACC. 27813</th>
<th>CHONDROBLASTOMA</th>
<th>Pages 2 - 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>CASE #2 - ACC. 27446</td>
<td>CHONDROSARCOMA</td>
<td>Pages 7 - 12</td>
</tr>
<tr>
<td>CASE #3 - ACC. 25658</td>
<td>DEDIFFERENTIATED CHONDROSARCOMA</td>
<td>Pages 13 - 17</td>
</tr>
<tr>
<td>CASE #4 - ACC. 27817</td>
<td>MESENCHYMAL CHONDROSARCOMA</td>
<td>Pages 18 - 22</td>
</tr>
<tr>
<td>CASE #5 - ACC. 27815</td>
<td>OSTEOBLASTOMA</td>
<td>Pages 23 - 27</td>
</tr>
<tr>
<td>CASE #6 - ACC. 27811</td>
<td>OSTEOSARCOMA</td>
<td>Pages 28 - 33</td>
</tr>
<tr>
<td>CASE #7 - ACC. 27806</td>
<td>TELANGIECTATIC OSTEOSARCOMA</td>
<td>Pages 34 - 37</td>
</tr>
<tr>
<td>CASE #8 - ACC. 27812</td>
<td>PERIOSTEAL OSTEOSARCOMA</td>
<td>Pages 38 - 42</td>
</tr>
<tr>
<td>CASE #9 - ACC. 27807</td>
<td>FIBROSARCOMA</td>
<td>Pages 43 - 47</td>
</tr>
<tr>
<td>CASE #10 - ACC. 27816</td>
<td>EWING'S SARCOMA</td>
<td>Pages 48 - 53</td>
</tr>
<tr>
<td>CASE #11 - ACC. 27814</td>
<td>MALIGNANT LYMPHOMA</td>
<td>Pages 54 - 59</td>
</tr>
<tr>
<td>CASE #12 - ACC. 27843</td>
<td>HEMANGIOPERICYTOMA</td>
<td>Pages 60 - 63</td>
</tr>
<tr>
<td>CASE #13 - ACC. 27818</td>
<td>ADAMANTINOMA</td>
<td>Pages 64 - 68</td>
</tr>
<tr>
<td>CASE #14 - ACC. 26787</td>
<td>CHORDOMA</td>
<td>Pages 69 - 73</td>
</tr>
<tr>
<td>CASE #15 - ACC. 23018</td>
<td>GIANT CELL TUMOR</td>
<td>Pages 74 - 78</td>
</tr>
<tr>
<td>CASE #16 - ACC. 27810</td>
<td>METASTATIC CARCINOMA</td>
<td>Pages 79 - 83</td>
</tr>
<tr>
<td>CASE #17 - ACC. 27764</td>
<td>ANEURYSMAL BONE CYST</td>
<td>Pages 84 - 88</td>
</tr>
<tr>
<td>CASE #18 - ACC. 25801</td>
<td>FIBROUS DYSPLASIA</td>
<td>Pages 89 - 93</td>
</tr>
<tr>
<td>CASE #19 - ACC. 27808</td>
<td>HISTIOCYTOSIS X</td>
<td>Pages 94 - 98</td>
</tr>
<tr>
<td>CASE #20 - ACC. 27809</td>
<td>BIZARRE PAROSTEAL OSTEOCHONDROMATOUS PROLIFERATION</td>
<td>Pages 99 - 102</td>
</tr>
</tbody>
</table>
CASE 1 - ACCESSION 27813

CHONDROBLASTOMA
Chondroblastoma is an extremely unusual neoplasm of bone accounting for less than 1 percent of bone tumors in the Mayo Clinic files. There is a definite male predominance. About 60 percent of the patients are in the second decade of life. Chondroblastomas occur at the ends of long bones centered in the epiphysis. They can also involve secondary centers of ossification such as the greater trochanter of the femur. They can be found in the small bones of the hands and feet. In a large series of cases reported by Dr. Kurt from the Mayo Clinic files, the talus and the calcaneus together form the single most common location. The region of the knee including the distal femur and the proximal tibia are the most common locations. The proximal humerus, where it was first recognized as a distinct entity, is almost as commonly involved as the proximal tibia. An unusual location is the temporal bone. Patients with involvement of the temporal bone tend to be older adults.

Local pain is the most common symptom. The other symptoms may be swelling and limb or joint stiffness. Physical examination may show a tender palpable area.

Roentgenograms characteristically show a central area of a refraction. The lesion extends to the articulate cartilage and typically extends through an open epiphyseal plate into the metaphysis. Rarely, a chondroblastoma will be purely metaphyseal. Typically, the area of lysis is surrounded by a thin sclerotic rim. Mineralization within the lesion is found in only one-third of the tumors.

Chondroblastomas tend to be small lesions grossly. They vary from 1 to 7 cm in greatest dimension. The gross appearance is not diagnostic. One usually can see fragments of gray material in which calcification may be identified. Occasionally, cystic change may be seen grossly.
Microscopically, chondroblastomas show proliferation of both mononuclear cells and benign giant cells. The mononuclear cells are considered to be chondroblasts. They tend to have well-defined cytoplasmic boundaries and an oval-shaped nucleus with a longitudinal groove in the center. This appearance is quite typical and practically diagnostic. Benign giant cells may be numerous or sparse. The giant cells usually contain 10 to 20 nuclei but may contain up to 40 or 50. In areas, the histological appearance is identical to that of a giant cell tumor. In order to make a diagnosis of a chondroblastoma, one has to identify either chondroid matrix or calcification. The chondroid matrix appears as islands of pink-staining cartilage adjacent to the proliferation of mononuclear cells. This is seen in over 90 percent of the cases. Calcification is in the form of fine lines between individual tumor cells. Calcification is found in approximately one-third of all cases. Some chondroblastomas will show epithelial-appearing cells with round nuclei and abundant pink cytoplasm.

Mitotic figures are commonly seen in the mononuclear cells. Sometimes the mononuclear cells will show bizarre nuclear features. Brown-yellow granular pigment, positive with ion stain, is present in approximately one-fourth of all cases of chondroblastoma. The pigment appears in the cytoplasm of the tumor cells. These are especially prominent in chondroblastomas involving the skull bone.

Foci of necrosis may be seen in chondroblastoma. Vascular invasion is extremely unusual. Secondary aneurysmal bone cysts occur within one-third of all chondroblastomas. This probably has no prognostic significance.

Chondroblastomas are generally treated with curettage with or without bone graft. Local recurrence may occur in 10 to 15 percent of cases. Some
chondroblastomas may have repetitive recurrences, become quite large, and are destructive. The term "aggressive chondroblastoma" may be used for this entity. I do not believe there are any histological features to support a separate designation of aggressive chondroblastoma. Chondroblastomas may metastasize to the lungs but with benign cytological features. Most of these metastases are solitary, well-circumscribed lesions, and their surgical removal results in a cure. There have been rare examples of chondroblastomas which have lead to progressive metastases and death of the patient.
REFERENCES


CASE 2 - ACCESSION 27446

CHONDROSARCOMA
Chondrosarcomas are the third most common primary neoplasm of bone after myeloma and osteosarcoma. They constitute approximately 9 percent of all malignant tumors in the Mayo Clinic files. There is a slight male predominance. Chondrosarcomas are predominantly a tumor of adulthood and old age. About 60 percent of the patients were in the fourth, fifth, and sixth decades of life. There were only five patients in the first decade of life in the Mayo Clinic files. The youngest patient was three years old. Patients with secondary chondrosarcoma, that is, chondrosarcoma arising in a preexisting condition, were somewhat younger.

Chondrosarcomas predominantly involve the trunk and the proximal portions of the humerus and femur. It is extremely unusual to see chondrosarcomas involving the distal portions of the skeleton such as the small bones of the hands and the feet. It is equally unusual to see chondrosarcomas involving the jaw and skull bones. Most chondroid neoplasms involving the maxilla and the mandible were the chondroblastic osteosarcomas. The majority of chondrosarcomas in the facial region involve the nasal bones.

Most patients present with swelling and pain. The presence of pain in a patient with a chondroid neoplasm is suggestive of malignancy. Physical findings depend upon the location of the lesion. Some chondrosarcomas become quite large and may be palpable.

Roentgenographic appearance of a chondrosarcoma may be diagnostic. Chondrosarcomas tend to be large. The majority of chondrosarcomas will show calcification. Occasionally, a chondrosarcoma will present as a purely lytic lesion in the medullary cavity. The earliest sign of malignancy in a chondrosarcoma is considered to be involvement of the cortex. The cortex is eroded from within producing a scalloped appearance.
In the later stages, the cortex appears thickened. As the cartilage tumor expands, it has a tendency to expand the involved bone. This combination of enlargement of the bone with thickening of the cortex is practically diagnostic of a chondrosarcoma.

Grossly, cartilage has a pale blue or white color. Areas of calcification may be identified as chalky areas. Chondrosarcomas tend to show myxoid change in the matrix. This manifests itself as a sticky mucinous quality to the gross specimen. If the myxoid change is pronounced, the matrix may undergo cystification. The presence of a chondroid neoplasm with cystic areas containing fluid in it is diagnostic of chondrosarcoma.

Microscopically, the differentiation of a low-grade chondrosarcoma from an enchondroma may be extremely difficult. The chondrosarcomas tend to show chondrocytes within lacunae in a blue-staining chondroid matrix. One of the cardinal features of malignancy is increased cellularity. This obviously is a subjective evaluation. Myxoid change in the matrix is a worrisome sign in a chondroid neoplasm. Myxoid change manifests itself as fraying of the matrix material. When there is marked myxoid change, the matrix may be lost. Double-nucleated cells are traditionally considered to be signs of malignancy. It is important to remember that the number of cells in a lacuna is not of any significance. One has to identify a cytoplasmic body and identify more than one nucleus in it. Increased nuclear size and hyperchromasia, as in any other kind of malignancy, are also important. Mitotic figures are hardly ever found in cartilaginous neoplasms. In my opinion, the most important sign of malignancy in a chondroid neoplasm is permeation. It is not unusual to see nodules of cartilaginous tissue in marrow cavity separate from the main mass even in benign chondroid
neoplasms. When there is true permeation, the narrow cavity is completely filled with the matrix material, and preexisting bony trabeculae are entrapped.

Grading of chondrosarcomas has prognostic significance. Chondrosarcomas are only graded from one to three. Chondrosarcomas are graded according to the cellularity of the neoplasm and the cytological atypia of the tumor cells. Grade 1 chondrosarcomas show increased cellularity and moderate nuclear atypia. Grade 2 chondrosarcomas are extremely cellular and show more pronounced cytological atypia. Grade 3 chondrosarcomas are unusual and show marked cellularity and nuclear anaplasia. In grade 3 chondrosarcomas, an occasional spindling nucleus may be seen. However, sheets of spindle cells rule out a diagnosis of chondrosarcoma.

There are several benign chondroid lesions which may mimic chondrosarcoma out of context. (1) Chondromas of the small bones of the hands and feet. These tend to be hypercellular, may show myxoid change, and large irregular nuclei. They may also show thinning of the cortex. However, experience suggests that these features are not diagnostic of chondrosarcoma in small bones. One has to see involvement of the soft tissues by the neoplasm before a diagnosis of chondrosarcoma in the phalanx is entertained. (2) Periosteal chondroma. Some chondroid neoplasms occur predominantly on the surface of bone. They tend to be small lesions, usually less than 5 cm in greatest dimension, and extremely well demarcated. Roentgenograms show a well-circumscribed lucent defect sitting in a depression in the cortex. Histologically, they may be hypercellular and show moderate cytological atypia. However, if the lesion is small, and the roentgenograms suggest a benign process, these cytological
features can be ignored. (3) Soft tissue chondroma. Soft tissue chondromas occur predominantly in the soft tissues of the hands and feet. They tend to be firm, lobulated masses involving the tendon sheath. Histologically, they tend to show increased cellularity and moderate nuclear atypia. These features can be ignored if the lesion is from a soft tissue. It is very unusual to see a chondrosarcoma of hyaline cartilage in soft tissue. (4) Synovial chondromatosis. Histological features of synovial chondromatosis are very similar to those of soft tissue chondroma. It tends to form nodules of cartilage within synovium. The lesion may be hypercellular and may show moderate to marked cytologic atypia. However, they tend to form clusters within synovium. This characteristic clustering quality is practically diagnostic of synovial chondromatosis. Sheet-like arrangements of chondrocytes are not seen in synovial chondromatosis.

Surgery is the mainstay in therapy of chondrosarcomas. Radiation and chemotherapy are not indicated. Surgery should be performed so that the entire lesion is removed in total with surrounding normal tissue. The prognosis in chondrosarcoma is excellent. It is unusual to see distant metastases with chondrosarcomas. Local recurrences may occur 10 to 15 years after treatment.
REFERENCES


CASE 3 - ACCESSION 25658

DEDIFFERENTIATED CHONDROSARCOMA
Approximately 10 percent of all chondrosarcomas of bone undergo a change into a high grade spindling malignancy which has been termed "dedifferentiated chondrosarcoma." The term "dedifferentiation" which was introduced by Dahlin and Beabout has been criticized as being biologically incorrect. Other cumbersome terms such as chondrosarcoma with an additional mesenchymal component have been suggested. However, the term "dedifferentiated chondrosarcoma" has gained acceptance in the literature and has the merit of being succinct. The concept is that a patient has a long-standing low grade chondrosarcoma which undergoes an abrupt transition into a high grade malignant tumor.

There are 120 cases of dedifferentiated chondrosarcoma in the Mayo Clinic files. At the same time, there were 1,020 chondrosarcomas. Patients with dedifferentiated chondrosarcoma tend to be somewhat older than patients with conventional chondrosarcoma.

The sites of involvement are similar to those of conventional chondrosarcoma, that is, towards the axial skeleton. The majority of tumors involve the pelvis, the proximal femur, and the proximal humerus. Patients generally complain of symptoms for a number of years.

The roentgenographic features of dedifferentiated chondrosarcoma may be diagnostic. The lesions tend to be large. Typically, the central portion of the lesion shows mineralization as seen in chondrosarcoma. The cortex may be thickened, eroded, or both. There usually is an unmineralized soft tissue mass adjacent to the mineralized portion. This juxtaposition of a very aggressive-looking lesion to what appears to be a conventional chondrosarcoma is typical of dedifferentiated chondrosarcoma. However, in about a quarter of the cases of dedifferentiated chondrosarcoma, the roentgenographic features suggest conventional chondrosarcoma.
The gross appearance of dedifferentiated chondrosarcoma may also be diagnostic. Typically, the central portion of the bone is filled with a characteristic pale blue cartilaginous material. Cystic change and myxoid change of the matrix may be seen. Juxtaposed to it is a fleshy tumor which has the appearance of a soft tissue sarcoma. The chondroid area and the fleshy areas do not intermingle.

The microscopic appearance of a dedifferentiated chondrosarcoma is that of a well-differentiated chondrosarcoma juxtaposed to a high grade spindle cell sarcoma. The cartilaginous areas may have obvious features of malignancy or may have the appearance of a borderline cartilage tumor. Typically juxtaposed to it is a high grade spindle cell sarcoma. This spindle cell portion may have the appearance of a fibrosarcoma, a malignant fibrous histiocytoma, or an osteosarcoma. When originally described, it was felt that the cartilaginous portion of the dedifferentiated chondrosarcoma should be extremely well differentiated. However, one can see some dedifferentiated chondrosarcomas in which the cartilaginous areas are obviously malignant and may be termed "grade 2."

The differential diagnosis includes a chondroblastic osteosarcoma and a mesenchymal chondrosarcoma. In chondroblastic osteosarcoma the chondroid areas are very malignant appearing and merge into a spindle cell malignancy. In dedifferentiated chondrosarcoma there is a sharp distinction between a reasonably well-differentiated chondrosarcoma and a high grade spindle cell sarcoma. In mesenchymal chondrosarcoma also, there are islands of cartilage and high grade malignant tumor. However, in mesenchymal chondrosarcoma, the high grade malignancy is represented by small malignant cells rather than the larger cells seen in dedifferentiated chondrosarcoma.
The treatment of dedifferentiated chondrosarcoma has been predominantly surgical. The lesion has to be removed completely regardless of what surgical procedure it entails. Chemotherapy has been tried in a few patients. The results have not been encouraging.

The prognosis in dedifferentiated chondrosarcoma is extremely poor. In the series reported by Frassica, the five-year survival rate was 10 percent. There are no long-term survivors with dedifferentiated chondrosarcoma in the Mayo Clinic files.
REFERENCES


CASE 4 - ACCESSION 27817

MESENCHYMAL CHONDROSARCOMA
Mesenchymal chondrosarcomas were first described by Lichtenstein and Bernstein in 1959. Primitive multipotential primary sarcoma of bone, as described by Hutter in 1966, includes lesions that fit the description of mesenchymal chondrosarcoma. Jacobson has used the term "polyhistioma" of bone and soft tissue to include small cell malignancies of bone producing both cartilaginous and osteoid matrix.

Mesenchymal chondrosarcomas are one of the rarest of bone tumors. They constitute less than one-third of one percent of all malignant bone tumors in the Mayo Clinic files. Until the end of 1993, there were only 34 patients with mesenchymal chondrosarcoma in the Mayo Clinic files. Only 25 of these involved the skeleton. Eight involved the soft tissue, and one involved the meninges. Although there was a slight male predominance in the Mayo Clinic series, in the larger series reported by Nakashima, there was a slight female predominance. Mesenchymal chondrosarcoma tends to affect young adults and teenagers. Approximately one-third of all patients are in the third decade of life.

As indicated previously, about one-third of all mesenchymal chondrosarcomas occur primarily in the soft tissues. Of the remainder, the jaw bone seemed to be the most common location. They also tend to involve the ribs, although any skeletal site may be involved. Patients generally complain of pain and swelling. The duration may be quite variable and may last up to seven years.

The roentgenographic features of mesenchymal chondrosarcoma are nondiagnostic. The majority show lytic destructive processes with or without mineralization. Many of the lesions show roentgenographic features of conventional chondrosarcoma such as calcification, expansion of bone, and cortical thickening. They are poorly marginated tumors suggesting a
malignancy. The gross pathological features are not diagnostic either. Generally, the lesion is soft and may show chalky areas of calcifications.

Histologically, mesenchymal chondrosarcoma is characterized by a bimorphic growth pattern. Islands of cartilage are juxtaposed to a small cell malignancy. When it was first described, it was thought that the islands of cartilage should look benign. However, over the years it has been realized that the chondroid areas may have the appearance of a low grade chondrosarcoma. The small cells usually have round to oval nuclei and have a very characteristic hemangiopericytomatic pattern. There are large vascular channels around which the small cells aggregate giving rise to a staghorn appearance to the vessels. Occasionally, the small cells may show spindling characteristics. The chondroid islands may undergo calcification or even ossification.

The differential diagnosis includes dedifferentiated chondrosarcoma, small cell osteosarcoma, and other small cell malignancies. As indicated previously in dedifferentiated chondrosarcoma, the high grade malignant cells are large, whereas in mesenchymal chondrosarcoma they are small cells. Small cell osteosarcoma generally does not show large areas of cartilage. If cartilage is present, they are in small foci and show high grade malignant features. Other small cell malignancies such as Ewing's sarcoma and malignant lymphoma should be ruled out on the presence of any matrix.

The treatment of mesenchymal chondrosarcoma is predominantly surgical. Because of its rarity, there is not much experience with chemotherapy. In the few cases that I have seen following chemotherapy, the response has not been good.

The prognosis in mesenchymal chondrosarcoma is unpredictable. Some patients present with disseminated disease and die very quickly. Other
patients live for a number of years with no evidence of disease only to get recurrent disease 15 or 20 years later and die of it. There are no histological features to predict prognosis.
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1. Lichtenstein L, Bernstein D: Unusual, benign, and malignant chondroid tumors of bone: a survey of some mesenchymal cartilage tumors and malignant chondroblastic tumors, including a few multicentric ones, atypical benign chondroblastomas and chondromyxoid fibromas. Cancer 12:1142-1157, 1959


CASE 5 - ACCESSION 27815

OSTEOBLASTOMA
In 1954 Dahlin and Johnson introduced the term "giant osteoid osteoma" to emphasize the similarity between osteoblastoma and osteoid osteoma. However, the term "osteoblastoma" as introduced by Drs. Jaffe and Lichtenstein. Osteoblastomas are extremely uncommon neoplasms. They account for <1 percent of all bone tumors in the Mayo Clinic files. They are one-third as common as osteoid osteoma.

Osteoblastoma tends to involve young patients, while 80 percent of the patients are in the first three decades of life. There is a marked male predominance.

Benign osteoblastoma tends to involve the vertebral column. Almost half of all lesions in the Mayo Clinic files involve the sacrum and the vertebrae. When they involve the vertebrae, osteoblastomas tend to involve the posterior elements. When long bones are involved, they tend to involve the medullary cavity, whereas osteoid osteomas tend to involve the cortex.

Patients present with pain which is usually progressive. Local swelling, tenderness, warmth, and gait disturbance may also be present. Osteoblastomas do not have the very characteristic symptom of being instantly relieved with aspirin that is associated with osteoid osteoma. Mirra and co-authors described a case of osteoblastoma associated with systemic toxicity.

The roentgenographic features of osteoblastoma are often nonspecific. The lesion may involve the metaphysis, the diaphysis, or less commonly, the epiphysis. They range in size from about 3 cm to 11 cm. The lesion may have the appearance of the nidus of an osteoid osteoma as a calcified center surrounded by a loosened halo. The nidus is usually over 2 cm in greatest dimension. More commonly, the lesions show a large area of destruction
with or without mineralization. The roentgenographic features may even suggest a malignancy.

The gross features of osteoblastoma are usually nondiagnostic. They usually present as red granular fragments.

Microscopically, osteoblastomas are composed of anastomosing bony trabeculae in a loose fibrovascular stroma. The lesion is extremely well circumscribed and does not show any permeation of preexisting structures. The bony trabeculae are variably calcified. There is a tendency for the center area to be less calcified than the periphery giving rise to a zonation phenomenon. The bony trabeculae are lined with a single layer of osteoblasts. The osteoblasts have round eccentrically placed nuclei and abundant pink cytoplasm. The nuclei may be quite prominent and may show a single prominent nucleolus. The stroma between the bony trabeculae is loose and quite vascular. Islands of cartilage may be seen rarely in an osteoblastoma.

The term "malignant osteoblastoma" was introduced to denote a lesion which had a tendency to recur locally. None of the cases thus described metastasized. Another term which has been introduced is "aggressive osteoblastoma." Aggressive osteoblastomas are characterized by the presence of epithelioid osteoblasts. These osteoblasts have abundant pink cytoplasm and prominent nucleoli. However, I have not been impressed that aggressive osteoblastoma forms a distinct clinicopathological entity. It is not unusual to see areas of epithelioid-appearing cells in an ordinary osteoblastoma. Even when one uses the criterion that all of the osteoblasts have to look epithelial, the clinical behavior does not seem to be different.

The differential diagnosis involves osteoid osteoma and osteosarcoma. Osteoid osteoma has a very characteristic symptom complex of pain, worse
at night, and relieved almost instantly with aspirin. Osteoid osteomas tend to involve the appendicular skeleton and very typically have a cortical location. The nidus is usually 1 cm or less and is composed of a mineralized center surrounded by a lucent halo. The cortex around the nidus is markedly thickened. The histological features of the nidus of osteoid osteoma and osteoblastoma are identical. The distinction is made on the size. Osteoid osteomas have a limited growth potential and do not grow beyond 1 cm in greatest dimension.

The distinction between an osteoblastoma and osteosarcoma can be extremely difficult. Most often osteosarcomas are underdiagnosed as osteoblastoma. This is because many osteosarcomas will have areas which are indistinguishable from those of an osteoblastoma. If the edge of the lesion is examined, osteosarcomas will always show permeation between preexisting bony trabeculae whereas osteoblastomas are well circumscribed. Osteoblastomas show a single layer of osteoblasts surrounding bony trabeculae whereas osteosarcomas will show sheets of osteoblast-like cells.

The treatment of osteoblastoma is surgical removal. Recurrence is a function of the surgery performed and not the histological features. The prognosis is excellent. Malignant transformation into osteosarcoma has been reported; however, this is extremely unusual.
REFERENCES


CASE 6 - ACCESSION 27811

OSTEOSARCOMA
Osteosarcoma can be simply defined as a malignant tumor of bone in which the tumor cells can be seen to produce either an osteoid or bony matrix at least focally. As of yet there is no special stain for osteoid. Hence, the division between hyalinized collagen and osteoids is arbitrary.

Using this definition, osteosarcoma is the second most common primary neoplasm of bone, second only to myeloma. It accounts for approximately 20 percent of all primary bone sarcomas.

There is a definite male predominance. The majority of patients with osteosarcoma are in the first two decades of life, especially in the second decade of life. It is unusual to see osteosarcoma below the age of five. However, 8 percent of the patients with osteosarcoma were above the age of 60. If an older patient is seen with an osteosarcoma, a preexisting condition such as Paget's disease should be suspected.

The metaphyseal region of the long bones is the site of predilection. Most osteosarcomas occur around the knee joint involving the distal femur and proximal tibia. It is extremely unusual to see osteosarcomas below the level of the ankle and wrist joints. Older patients are more likely to get involvement of the axial skeleton with osteosarcoma.

Pain and swelling are the cardinal symptoms. It is unusual to see osteosarcoma present with a pathological fracture. Physical examination usually reveals a painful mass in the affected area.

The roentgenographic appearance of osteosarcoma varies greatly depending upon the amount of ossification and calcification in the tumor. The tumor may be completely lytic or may be sclerotic but usually shows a mixture of both. The tumors tend to be large and poorly demarcated. The cortex is usually destroyed by the time the patient has a diagnosis, and a large soft tissue mass may be present. As the tumor grows through the
cortex, the periosteum is lifted giving rise to reactive new bone formation. This has been termed "Codman's triangle." Plain roentgenogram is still the best medium for diagnosing osteosarcoma prior to biopsy. Newer modalities such as MRI and CT do not add significantly to the diagnosis. However, they do add significantly in determining the extent of the neoplasm. With the advent of limb salvage surgery, knowledge about the extent of the disease has become even more critical.

Grossly, the tumor has usually broken through the cortex to form a soft tissue mass by the time diagnosis is made. The extrasosseous mass may even completely encircle the bone. The gross appearance may suggest a fleshy neoplasm such as seen in most sarcomas or may be distinctly chondroid appearing. A small number of osteosarcomas show extreme ossification so the tumor may have the texture of cortical bone.

The histopathological features of osteosarcoma vary greatly. However, the tumor must produce matrix at least focally. Approximately 50 percent of osteosarcomas can be considered to be osteoblastic osteosarcomas. Highly malignant-appearing cells, usually spindle shaped, produce large amounts of matrix. Osteoid has a pink hyaline quality. Characteristically, the osteoid is in the form of a fine lace-like network between individual tumor cells. The tumor cells themselves may be spindle shaped, epithelioid appearing, or even small cells. In any event, they show high grade cytological changes. The matrix will occasionally become organized into trabeculae of bone. Even more rarely, so much matrix is produced that the tumor appears to be matrix with few if any cells. A diagnosis of osteosarcoma is made in this situation if only the matrix can be seen to fill up the marrow cavity entrapping preexisting trabeculae of bone.
About a quarter of all osteosarcomas will show a predominant chondroid differentiation. The cartilage is in the form of lobules, and the tumor cells are in lacunae. However, the chondrocytes show marked cytological atypia. Towards the periphery of the lobules, the tumor becomes quite hypercellular and the tumor cells spindle out. Matrix material is seen between the individual spindling tumor cells. Occasionally trabeculae of bone are seen within the lobules of cartilage. The remaining high grade osteosarcomas may be termed "fibroblastic osteosarcomas." These show spindle cell tumors with only focal production of osteoids.

Most of the conventional osteosarcomas can be divided into osteoblastic, chondroblastic, or fibroblastic varieties. This subclassification probably has no prognostic significance. However, some variation may be seen even in these types. Benign giant cells are commonly found in osteosarcomas. Usually they form an insignificant portion and do not cause diagnostic difficulties. Once in a while, however, one will see an osteosarcoma which has so many benign giant cells that a diagnosis of a giant cell tumor may be entertained. It is important to consider the possibility of an osteosarcoma if the clinical features, such as the location within bone, indicate an osteosarcoma, but the biopsy shows what appears to be a giant cell tumor.

Some osteosarcomas will have very epithelioid-appearing cells. Even gland-like formations may be seen in osteosarcoma. If an epithelial-appearing neoplasm occurs in an age group where metastatic carcinoma is practically impossible, the diagnosis of osteosarcoma should be suspected.

The treatment of osteosarcoma has undergone great changes over the last few years. Before the advent of chemotherapy, immediate amputation
was the treatment of choice. Now, most patients with osteosarcoma do not undergo amputation. A biopsy diagnosis is made, and the patient is treated with preoperative chemotherapy. The majority of patients undergo some sort of limb salvage surgery after preoperative chemotherapy. Several studies have suggested that the amount of necrosis seen after preoperative chemotherapy correlates extremely well with prognosis in osteosarcoma. I usually take one entire slice of the tumor with the attached bone and decalcify it. This may take up to a week because of the cortical bone present. The entire specimen is then embedded in multiple blocks. A map of the tumor can be made by examining the slides. Necrosis may be manifested as a necrotic-looking tumor, inflammatory granulation tissue, or extensive ossification. It appears that 95 percent or more necrosis of the tumor is associated with a good prognosis. Hence, it is probably not important to try and be exact about the percentage of necrosis if it is over 10 percent or so.
REFERENCES


CASE 7 - ACCESSION 27806

TELANGIECTATIC OSTEOSARCOMA
Telangiectatic osteosarcoma is an unusual neoplasm. Of a total of 1,786 osteosarcomas in the Mayo Clinic files, only 57 were considered to be telangiectatic. The criteria for making the diagnosis are as follows: (1) the roentgenogram shows a purely lytic destructive lesion. Any appreciable sclerosis within the lesion rules out a diagnosis of telangiectatic osteosarcoma. Although all telangiectatic osteosarcomas are purely lytic, all purely lytic osteosarcomas are not telangiectatic. (2) Grossly, the tumor has the appearance of a bag of blood. Large areas of flesh-like tumor tissue or sclerotic sarcoma are not seen. (3) Microscopically, two patterns are seen. Most of the tumors have the appearance of an aneurysmal bone cyst on low power. Spaces containing blood are separated by septa. Benign giant cells are almost always found. The cells lining the septa show very pleomorphic nuclei. Normal and abnormal mitotic figures are commonly found. Osteoid production is minimal. The second pattern is that of highly anaplastic-looking cells with no pattern apparently floating in blood.

The differential diagnosis obviously involves aneurysmal bone cysts and giant cell tumors. Most telangiectatic osteosarcomas occur in the metaphysis whereas giant cell tumors occur in the epiphysis. In my experience all telangiectatic osteosarcomas are high grade malignancies, and hence, cytological atypia is obvious. The roentgenographic clinical and low power appearance of telangiectatic osteosarcoma may be identical to that of an aneurysmal bone cyst. However, the lining cells look obviously malignant in telangiectatic osteosarcoma, whereas they are clearly benign in aneurysmal bone cysts.

The original report from the Mayo Clinic by Dr. Matsuno in 1976 suggested that the prognosis in telangiectatic osteosarcoma was worse than for conventional osteosarcoma. At that time there were 25 patients with
telangiectatic osteosarcoma in the Mayo Clinic files. Of these, 23 were dead. One patient was alive with metastasis, and only one patient was alive up to five years. The patient who was alive up to five years subsequently died of metastatic disease. The patient who was alive with metastasis is still alive at about 17 years following multiple surgical procedures for removal of metastatic disease. Since that report, however, the prognosis in telangiectatic osteosarcoma seems to be the same as for conventional osteosarcoma. This is similar to the experience from Memorial Hospital in New York. Indeed, telangiectatic osteosarcoma seems to be extremely sensitive to chemotherapy.
REFERENCES


CASE 8 - ACCESSION 27812

PERIOSTEAL OSTEOSARCOMA
The majority of osteosarcomas arise within the bone. A small minority appear to occur predominantly on the surface of bone. The surface osteosarcomas can be divided into three distinct subgroups depending upon roentgenographic, clinical, and histologic features. (1) Parosteal osteosarcoma. Parosteal osteosarcoma was the earliest recognized type of osteosarcoma which occurs on the surface of bone. Although it is the most common type of surface osteosarcoma, there were only 69 examples in the Mayo Clinic files out of a total of 1,786 osteosarcomas. The tumor tends to involve young and older adults. There is a distinct female predilection. Patients complain of a painless swelling which may have been present for a number of years. The most common location is the distal femur posteriorly. This accounts for about 70 percent of all tumors. Because of this location, patients may complain of inability to flex the knee.

Roentgenograms usually show a very heavily mineralized mass on the surface of the bone. It is attached to the underlying cortex but is not continuous with the medullary cavity. It is usually attached with a broad base, and as the tumor grows, it grows away from the underlying bone giving rise to a lucency between the neoplasm and the bone. The periphery of the lesion is usually less mineralized than the central portions.

Grossly, the tumor is attached to the cortex but does not show involvement of the medullary cavity. The tumor may be large and may actually wrap around the underlying bone. It is hard to firm. Much of the tumor may be so heavily ossified that sections cannot be cut without decalcification. The peripheral areas are softer, and skeletal muscle fibers may be incorporated into the neoplasm.

Microscopically, parosteal osteosarcoma is an extremely well-differentiated osteosarcoma. Bony trabeculae simulating those seen in
normal bone are present. The intertrabecular spaces are filled with a hypocellular spindle cell proliferation. The spindle cells are separated by abundant collagen. The nuclei do not show marked cytological atypia, and mitotic figures are sparse. Gross or microscopic evidence of medullary invasion may be seen in about one-third of the cases.

The treatment of parosteal osteosarcoma is surgical. If the lesion is removed completely, the prognosis is excellent. Distant metastases are distinctly uncommon. About 15 percent of parosteal osteosarcomas will undergo dedifferentiation into a high grade osteosarcoma. This may arise de novo or at the time of recurrence. In either event, the prognosis is that of a high grade osteosarcoma.

Periosteal osteosarcoma. Periosteal osteosarcoma, also known as juxtapartical chondrosarcoma, forms the second largest group of surface osteosarcomas. There were only 26 examples in the Mayo Clinic files until the end of 1993. Skeletal and age distribution are similar to those of conventional osteosarcoma. However, there is a tendency to involve the diaphysis of the bone rather than the metaphysis. There is a distinct female predominance.

The roentgenograms show a lucent defect on the surface of the bone. The cortex may appear saucerized. The lucency merges into surrounding soft tissue. Perpendicular areas of mineralization giving rise to a sunburst appearance may be present within the lesion. However, periosteal osteosarcomas do not show the heavy mineralization characteristic of parosteal osteosarcoma.

Grossly, periosteal osteosarcomas show the light blue appearance of cartilage. The medullary cavity should not be involved. Microscopically, periosteal osteosarcoma is a moderately differentiated chondroblastic
osteosarcoma. The tumor is composed of lobules of cartilage with peripheral spindling. Very typically, trabeculae of bone are present within the center of the lobules of cartilage giving rise to a feathery appearance. Lace-like osteoids may be seen in the peripheral spindling areas also. I believe that the histological features of periosteal osteosarcoma are typical but are not diagnostic. Any chondroblastic grade 3 osteosarcoma can look like a periosteal osteosarcoma. Hence, I believe that in order to make a diagnosis of periosteal osteosarcoma, one has to insist that the medullary cavity be not involved.

The prognosis in periosteal osteosarcoma is excellent. Only 5 of the 26 patients in the Mayo Clinic files have died of disease. Seventeen patients are alive from 4 to 32 years after treatment. Whether chemotherapy is required in the treatment of periosteal osteosarcoma is still unclear.

High grade surface osteosarcoma. Very rarely a highly anaplastic osteosarcoma occurs predominantly on the surface of bone. There were only 12 such examples in the Mayo Clinic files. Roentgenograms usually show the tumor to be confined to the surface of bone. The roentgenographic features are nonspecific and may even suggest a diagnosis of periosteal osteosarcoma. Microscopic foci of medullary involvement are commonly seen. The histological features are those of a high grade osteosarcoma, very similar to that of conventional osteosarcoma. The follow-up confirms that it is important to separate high grade surface osteosarcoma from periosteal osteosarcoma. Nine of the twelve patients with high grade surface osteosarcoma died of disease.
REFERENCES


CASE 9 - ACCESSION 27807

FIBROSARCOMA
Fibrosarcoma of bone can be defined as a malignant spindle cell tumor that does not produce osteoid or cartilaginous matrix. Collagen is produced and varies depending upon the grade of the tumor. High grade fibrosarcomas tend to produce less collagen than low grade tumors. The differentiation from fibroblastic osteosarcoma is somewhat arbitrary.

In the Mayo Clinic files, fibrosarcoma is only about one-sixth as common as osteosarcoma. Males and females are about equally affected. Fibrosarcomas do not show the marked propensity for young patients as osteosarcoma. The incidence is more or less evenly distributed throughout the age groups.

The sites involved by fibrosarcomas do not differ from those involved by osteosarcomas. The region around the knee that includes the distal femur and the proximal tibia was the most common location. Approximately 50 percent involve long bones where they are situated in the metaphyseal region. The symptoms and physical findings are not remarkable.

Roentgenograms generally show a purely lytic destructive process. The majority of fibrosarcomas show poorly defined margins, cortical destruction, and soft tissue extension, all features of malignancy. However, occasionally a fibrosarcoma will show well-defined margins suggesting a benign process. There essentially are no differences in the roentgenographic features of fibrosarcoma, fibroblastic osteosarcoma, and malignant fibrous histiocytoma.

The gross features are those of a spindle cell sarcoma of soft tissue. High grade tumors tend to be soft and fleshy, whereas low grade tumors tend to be fibrous and firm.

Fibrosarcoma of bone has the same histologic features as its soft tissue counterpart. On low power, the lesion appears to permeate bone marrow.
Fibrosarcomas are graded according to the cellularity and the cytological features of the neoplasm. Low grade tumors tend to show minimal cytological atypia, sparse mitotic activity, and abundant collagen production so that the entire lesion is distinctly hypocellular. It may be impossible to make a diagnosis of malignancy on a limited tissue sample. The most reliable sign of malignancy is the permeation of preexisting bony trabeculae. Grade 2 fibrosarcomas tend to show increased cellularity and more cytological atypia. Mitotic figures may be found. Grade 3 fibrosarcomas are quite cellular with little collagen production, and the nuclei show marked atypia. Grade 4 fibrosarcomas are pure cellular growths with little or no collagen production. Mitotic figures may be abundant, and the nuclei tend to show marked atypia.

Fibrosarcomas, almost by definition, do not show marked pleomorphism. Benign giant cells are also unusual in fibrosarcoma. Although all spindle cell sarcomas are graded 1 to 4 for practical purposes, it is only necessary to grade it into low grade and high grade types. Grade 1 and 2 will be combined into low grade, and grade 3 and 4 will be combined into high grade. Several studies have shown that this has prognostic significance.

Some fibrosarcomas have a prominent myxoid component. This may make the lesion hypocellular and suggest a benign process. Some fibrosarcomas will have extremely small cells, and on limited material, a diagnosis of Ewing's sarcoma may be made. If the tumor cells can be shown to be truly spindle shaped, a diagnosis of Ewing's sarcoma is not tenable.

Metastatic spindling carcinoma should be in the differential diagnosis whenever a diagnosis of fibrosarcoma is made. It is reasonable to think of the possibility of sarcomatoid carcinoma if the lesion occurs in the age group where sarcomatoid carcinomas occur. In my experience
hypernephroma is the most common primary neoplasm which can mimic a primary fibrosarcoma of bone. For practical purposes it is important to clinically rule out the possibility of hypernephroma before definitive treatment is undertaken.

Fibrosarcomas are not distinctly different from malignant fibrous histiocytoma or osteosarcoma. Treatment has generally been surgical. There is not enough experience with chemotherapy to learn of its effectiveness.

The prognosis in fibrosarcomas is similar to that of osteosarcoma and malignant fibrous histiocytoma. The grade of the neoplasm affects prognosis.
REFERENCES


CASE 10 - ACCESSION 27816

EWING'S SARCOMA
Ewing's sarcoma is a distinctive small round cell sarcoma of bone. The diagnosis of Ewing's sarcoma has generated a lot of controversy. In the past the controversy involved whether all Ewing's sarcomas were in fact metastatic neuroblastomas. More recently, the controversy involves the so-called primitive neuroectodermal tumor. For practical purposes, Ewing's sarcoma is a primary small round cell sarcoma of bone without matrix production.

Ewing's sarcoma is about one-fourth as common as osteosarcoma. It accounted for approximately 9 percent of all primary sarcomas of bone in the Mayo Clinic files. As with many bone tumors, it has a distinct predilection for males. Patients with Ewing's sarcoma are distinctly younger than patients affected with other primary neoplasms of bone. Over 50 percent are in the second decade of life, and 75 percent are in the first two decades of life. However, it is unusual to see Ewing's sarcoma below the age of five, an age group where metastatic small cell malignancies such as neuroblastoma are more common. It is also distinctly unusual to see Ewing's sarcoma in an older individual. If such a diagnosis is entertained in an older individual, metastatic small cell malignancies such as small cell carcinoma of the lung have to be excluded.

Most Ewing's sarcomas occur in the extremities. The lower extremities and pelvic girdle accounted for about 60 percent of all tumors in the Mayo Clinic files. The ribs, however, were the third most common site of involvement. In long bones the tumor tends to involve the metaphysis, although the diaphysis is more commonly involved than with other sarcomas.

Pain and swelling are the most common symptoms with Ewing's sarcoma. The patients may present with systemic symptoms and signs such
as anemia, fever, and weight loss. Erythrocyte sedimentation rate may also be elevated. All of these features may suggest a diagnosis of osteomyelitis.

Roentgenograms tend to show extensive involvement of bone. The entire shaft of the bone may be involved with Ewing's sarcoma. Lytic destruction of bone is common. The tumor may grow as small lytic areas in bone giving rise to a permeative appearance. Some tumors give rise to large geographic areas of destruction. Most often the tumor has invaded soft tissues by the time a clinical diagnosis is made. Ewing's tumor characteristically and has extensive periosteal new bone formation. This new bone formation may be in the form of layers giving rise to an onion skin appearance. Some Ewing's sarcomas may show mixture of lysis and sclerosis because of the presence of reactive new bone formation. In these instances it may be impossible to differentiate the neoplasm from osteosarcoma on roentgenographic grounds.

Ewing's sarcoma tends to be a very soft white neoplasm which may have the appearance of pus. This may lead to the surgeon mistaking the process for osteomyelitis and sending all the biopsy material for microbiological studies.

Ewing's tumor is a cellular neoplasm because of lack of matrix. The cells are small, round, and more or less uniform. Cytoplasmic boundaries are indistinct. Areas of necrosis may be prominent. The nuclei are quite uniform. An occasional dark-staining nucleus may be seen. True spindling of the nuclei should not be found. There may be crush artifact at the edges of a biopsy which may give rise to artifactual spindling.

Mitotic figures are not commonly found in Ewing's sarcoma, although it is a very high grade neoplasm. About 5 to 10 percent of Ewing's sarcomas will have larger more irregular nuclei. These large cell or atypical Ewing's
sarcomas tend to show more mitotic activity than conventional Ewing's sarcoma. This distinction apparently does not have any clinical significance.

Because of the somewhat nonspecific nature of the neoplasm, attempts have been made to develop a special stain to make the diagnosis. In 1959, Schajowicz advocated the use of glycogen stain in differentiating Ewing's sarcoma from malignant lymphoma. He pointed out that the cells of Ewing's sarcoma contained abundant glycogen in the cytoplasm. Electron microscopy also confirmed the presence of abundant glycogen in the cytoplasm of the cells of Ewing's sarcoma. I have not personally found it very useful in diagnosing Ewing's sarcoma. Lately, a stain termed "HBA-71" which recognizes a product of MIC-2 gene has been suggested to be specific for Ewing's sarcoma. However, further studies have demonstrated that this stain is not as specific as first thought.

Several studies have confirmed a characteristic 11-22 chromosomal translocation in Ewing's sarcoma. The same translocation has been found in primitive neuroectodermal tumor. The term "primitive neuroectodermal tumor" is used when a small cell malignancy shows a tendency to form rosettes. It does not appear as if this has any prognostic significance.

The differential diagnosis involves all kinds of small cell malignancies. Metastatic neuroblastoma usually occurs in the first two years of life when Ewing's sarcoma is distinctly uncommon. It is unusual for metastatic neuroblastoma to present without a known primary. Most often the cytologic features are so characteristic with the production of fibrils in the background that the differential diagnosis is not difficult. However, occasionally one will find a neuroblastoma in which the cells do not show the differentiation that would allow for easy recognition. If a bone biopsy
shows extensive crush artifact in a small child, I consider the possibility of metastatic neuroblastoma and a lymphoblastic leukemia.

In a small percentage of patients, it might be difficult to separate lymphoma from Ewing's sarcoma. Most lymphomas show more polymorphism than is seen in Ewing's sarcoma. However, simple stains such as common leukocyte antigens should resolve this dilemma.

The treatment of Ewing's sarcoma has undergone dramatic changes recently. The advent of radiation and chemotherapy has changed the prognosis from a very dismal 5 to 10 percent to about 50 to 60 percent survival. The prognosis seems to be better in patients who have been treated with surgery in addition to radiation and chemotherapy.
REFERENCES


CASE 11 - ACCESSION 27814

MALIGNANT LYMPHOMA
Malignant lymphoma may involve bone as a primary osseous neoplasm or as an osseous manifestation of systemic lymphoma. This distinction has prognostic significance.

Malignant lymphoma was found in approximately 8 percent of all malignant bone tumors in the Mayo Clinic files. Males predominate in a ratio of 4 to 3. It is unusual to see malignant lymphoma of bone in very young patients. There were only 19 patients in the first two decades of life in the Mayo Clinic files. Malignant lymphoma of bone is most common in young and older adults.

Most lymphomas of bone involve a portion of the skeleton containing red marrow. Hence, it is unusual to see lymphoma involving the distal portions of the skeleton. The femur and the ileum were the most common sites.

Pain and swelling are common symptoms. With involvement of the spine, neurological symptoms may predominate. Patients also may have systemic symptoms suggesting involvement of lymphoma in other organs. Physical examination may reveal a warm tender mass. Regional lymph nodes may be involved.

Roentgenograms usually show extensive involvement of the bone. Usually the mid portion of the bone is involved. Areas of destruction give the bone a mottled and patchy appearance. The outline of the bone may be completely lost. Frequently there is reactive sclerosis within the bone so that the appearance is that of a mixture of lysis and sclerosis. The cortex is usually destroyed, and there may be a large soft tissue mass. Periosteal new bone formation is distinctly unusual in malignant lymphoma. When the destruction is confined to the medullary cavity, there may be extensive involvement of the bone which may not be obvious on plain
roentgenograms. Radioactive bone scans are usually positive at these sites. Magnetic resonance images also highlight the marrow involvement. Positive findings on bone scan or MRI associated with a negative plain x-ray is suggestive of malignant lymphoma.

The gross features of malignant lymphoma of bone are similar to those of lymphoma elsewhere. The lesion is soft, fleshy, and white. Almost without exception, lymphoma of bone has a diffuse growth pattern rather than a follicular one. On low power, the tumor invades fatty marrow leaving behind normal structures which is a characteristic pattern of growth of lymphoma in any organ. Most lymphomas of bone show a mixed cell infiltrate in the sense that there is polymorphism of the invading nuclei. Very characteristically, there is a very fine fibrosis present between individual tumor cells. Crush artifact is commonly found in a lymphoma of bone. Such crush artifact is much more common in lymphoma than in Ewing's sarcoma. Classification of lymphoma of bone is difficult because of the mixed cell infiltrates. Because of the fibrosis presented in the lesion, sometimes the cells tend to spindle out. This may give rise to a mistaken diagnosis of sarcoma. Sometimes the tumor cells cluster suggesting an epithelial neoplasm: Immunoperoxidase stains for a common leukocyte antigen and are helpful in differentiating lymphoma from metastatic carcinoma and sarcoma.

Hodgkin's disease may appear as a skeletal process. Most often the involvement is secondary to a known Hodgkin's disease. Even when skeletal involvement is a presenting sign of Hodgkin's disease, it is unusual to see solitary skeletal disease. The most common site of involvement of Hodgkin's disease is the vertebrae. Most often the para-aortic lymph nodes are also involved. Whenever a lymphoma with a mixed infiltrate and large
pleomorphic nuclei are seen, the possibility of Hodgkin's disease should be entertained. Immunoperoxidase stains for BER-H2 and LEU-M1 are helpful stains in confirming the diagnosis of Hodgkin's disease. Leukemic infiltrates may also present as a bony mass. Granulocytic sarcoma may present as a destructive tumor of bone. The histological features may be suggestive of a large cell lymphoma. Imprints stained with Wright's stain may be helpful in differentiating granulocytic sarcoma from malignant lymphoma. If precursors such as eosinophilic myelocytes are seen, the possibility of granulocytic sarcoma should be considered. Immunoperoxidase stains such as myeloperoxidase should be used to confirm the diagnosis of granulocytic sarcoma. The lesion may not be associated with involvement of the bone marrow.

The treatment of malignant lymphoma involves radiation and chemotherapy. The prognosis depends more on the stage of the disease than the exact histologic subclassification. When a diagnosis of malignant lymphoma of bone is made, four clinical situations may apply. (1) The biopsy diagnosis of malignant lymphoma of bone is made. Extensive investigation does not reveal evidence of disease elsewhere in the body. This may be termed "primary lymphoma of bone." This is associated with an excellent prognosis. (2) The patient may have multiple sites of involvement in the skeleton. This is demonstrated best by radioactive bone scan. However, there is no disease elsewhere in the body such as the lymph nodes. Even though this may be considered to be stage IV disease, it is usually associated with a surprisingly good prognosis. (3) The patient's diagnosis is made from a bone biopsy. However, workup reveals evidence of disease elsewhere such as in lymph nodes. The prognosis in this clinical situation is not good. (4) The patient has a known malignant lymphoma...
perhaps of a lymph node. Bone biopsy is done to confirm involvement of the skeleton. This clinical situation is associated with a very poor prognosis.
REFERENCES


CASE 12 - ACCESSION 27843

HEMANGIOPERICYTOMA
Hemangiopericytoma is one of the rarest of primary bone neoplasms. There were only 13 examples in the Mayo Clinic files until the end of 1993. Of these 13 patients, 8 were male, and 5 were females. The peak incidence was in the fourth decade of life. Any portion of the skeleton may be involved, but the most common site was the ileum.

The clinical symptoms are nonspecific. Patients usually complain of localized pain.

The roentgenographic appearance also is nonspecific. It usually presents as a purely lytic expansile lesion.

The gross appearance of hemangiopericytoma is not pathognomonic. The lesion is usually firm and may feel rubbery. The surgeon may encounter catastrophic bleeding at the time of surgery.

The histologic features of hemangiopericytoma of bone are identical to those of the soft tissue counterpart. The tumor cells are round to oval. Although focal areas of spindling may be seen, hemangiopericytoma is not a spindle cell neoplasm. The tumor cells do not show marked pleomorphism. Tumor cells are arranged very characteristically around vascular spaces which are deformed by the proliferating tumor cells to give rise to unusual shapes. The vascular spaces very characteristically have a deer antler appearance. Reticulin stains may highlight occult blood vessels.

This pattern of intimate relationship between the tumor cells and the vessels should be present throughout the lesion. Focal hemangiopericytomaticus patterns may be seen in a number of spindle cell malignancies. Osteosarcomas, malignant fibrous histiocytomas, and fibrosarcomas may all show focal hemangiopericytomatic patterns. Mesenchymal chondrosarcoma very typically shows a hemangiopericytomatic pattern. However, the tumor cells in
hemangiopericytoma are not as atypical appearing as those seen in mesenchymal chondrosarcoma. The presence of any matrix such as cartilage or bone should rule out the possibility of hemangiopericytoma.

Metastatic hemangiopericytoma should always be in the differential diagnosis when a biopsy shows a hemangiopericytoma of bone. Hemangiopericytoma of the meninges, also known as vascular meningioma, has a tendency to metastasize to bone.

The treatment is surgical. There is not enough information in the literature about effect of radiation and chemotherapy. I think all hemangiopericytomas should be considered potentially malignant. Very benign-appearing ones may be associated with long-term survival.
REFERENCE

CASE 13 - ACCESSION 27818

ADAMANTINOMA
Adamantinoma of long bone is a peculiar neoplasm that occurs almost exclusively in the tibia. The name adamantinoma comes from its histological resemblance to the more common ameloblastoma of the jaw bones.

Adamantinoma forms approximately one-third of one percent of all primary malignant bone tumors in the Mayo Clinic files. In the Mayo Clinic files, male and female patients were equally represented. Most patients with adamantinoma are adolescent and young adults. About three-fourths of the patients are in the second and third decades of life. The youngest patient was seven years old, and the oldest was 79.

Of all reported adamantinomas of long bones, 90 percent have involvement of the tibia. However, rare tumors have been reported in other large bones. A small percentage of patients will have involvement of both the tibia and the fibula. Occasionally the patient will present with a lesion of the fibula and develop the tumor of the tibia years later. Very typically the tumor involves the mid portion of the tibia.

Most patients present with pain. The duration of symptoms may be prolonged. One of the patients in the Mayo Clinic files had roentgenographic evidence of disease for 50 years before a diagnosis was made. At least one-third of all patients will have symptoms for over five years. Physical examination may reveal a painful mass.

The roentgenographic appearance of adamantinoma is usually quite typical. The lesion tends to involve the cortex and the medullary cavity. The shaft of the bone is involved, and the lesion is presented as multiple areas of bone destruction interspersed with sclerotic bone. There usually is a large area of destruction in the mid portion. Some tumors may present as a nonspecific area of destruction.
Grossly, adamantinomas are usually well circumscribed. They present as soft white masses within the cortex but also involve the medullary cavity. The cortex may be destroyed with extension of the neoplasm into soft tissue.

The histological feature is quite variable, but the essential feature is an epithelial quality of the tumor cells. The typical histological appearance is of small epithelial islands in a fibrous stroma. The epithelial islands have the features seen in ameloblastoma. That is, a central loose area surrounded by palisading columnar cells. The amount of epithelial cells in relation to the fibrous tissue may be quite variable. Some tumors have a predominant fibrous stroma with bone formation. These areas may resemble the appearance of fibrous dysplasia or osteofibrous dysplasia. Epithelial islands may be present as inconspicuous areas within the fibrous proliferation. Other lesions show prominent epithelial islands with little fibrous stroma. Rarely the tumor has a pure spindle cell quality. If a spindle cell neoplasm is seen in the cortex of the tibia, the diagnosis of adamantinoma should be made. Whatever the histological characteristics are, one essential factor is that the tumor cells lack marked cytological atypia.

It has been known for a long time that some adamantinomas have a vascular appearance. Anastomosing channels similar to that seen in vascular neoplasms may be seen merging into obviously epithelial cells. Clear-cut squamous cell differentiation and keratin production are unusual.

The differential diagnosis involves metastatic carcinoma and a fibrosarcoma. It is unusual to see metastatic carcinoma below the level of the knee joints. Moreover, patients with adamantinoma are distinctly younger than patients with metastatic carcinoma. Most importantly, adamantinomas lack the pronounced cytological atypia usually seen in
metastatic carcinoma. When the tumor is purely spindle shaped, a fibrosarcoma may be in the differential diagnosis. However, adamantinomas do not produce collagen as fibrosarcomas do. They do not have the cytological atypia of high grade fibrosarcoma. Keratin stains will stain the tumor cells positively in adamantinoma, whereas they do not stain the cells of fibrosarcoma.

The treatment of adamantinoma is surgical. Because of the extensive nature of involvement, it may be necessary to do an amputation. With advances in limb salvage surgery, resection has become a viable option. Prognosis in adamantinoma is excellent. However, recurrences may be delayed. Metastasis may be hematogenous or into regional lymph nodes.
REFERENCES


CASE 14 - ACCESSION 26787

CHORDOMA
Chordoma accounted for approximately 4 percent of all malignant tumors of bone in the Mayo Clinic files. It affects males much more commonly than females. Chordoma is very uncommon in patients younger than 30 years of age. In the Mayo Clinic files, there were only four patients in the first decade of life with chordoma, and they all had involvement of the sphenoid region. The youngest patient with involvement of the sacrum was a 20-year-old man.

Chordoma always involves the midline. In the recent Mayo Clinic files, 47 percent of the lesions involve the sacrum, 38 percent involve the spheno-occipital occipital region, and the remainder involve the spinal column. The cervical spine is most commonly involved when the disease affects the spinal column.

The duration of symptoms varies from months to several years. Pain is a constant symptom of sacrococcygeal chordoma. Patients may present with constipation or other neurological symptoms such as bladder dysfunction. Because of the overlying gas shadows, plain roentgenograms may miss a chordoma of the sacrum for a long time. Patients with spheno-occipital chordoma present with cranial nerve paralysis.

Sacroccygeal chordomas very characteristically present as a presacral mass and may be felt on a rectal examination. Chordomas on the base of the brain may produce neurologic deficits.

Roentgenographic features depend on the site of involvement. The one constant feature is the involvement of the midline. A soft tissue mass is usually present anteriorly. With more modern imaging techniques such as CT and MRI, sacral chordomas are better defined nowadays. Spheno-occipital chordomas always involve the clivus. Chordomas of the rest of the spine produce destructive lesions of the vertebral body.
Grossly, a chordoma is a soft lobulated grayish tumor. It has a semitranslucent appearance.

Microscopically, chordoma is always a lobulated neoplasm. If sufficient tissue is obtained, nodules of tumor separated by fibrous septa are found. Chordomas stain blue because of the myxoid background in the tissue. The tumor cells are usually small, round, and do not show pronounced cytological atypia. They are embedded in a myxoid matrix forming chords. Tumor cells frequently will contain abundant cytoplasm which may be avacuolated giving rise to the term "physaliferous cells." Some chordomas may have spindle cells. Some chordomas may show bizarre nuclear features. These characteristics are not associated with difference in prognosis.

Chondroid chordoma is a term which has led to much controversy. This was first described by Heffelfinger and co-authors in a study of chordomas of the base of the skull. These authors found that chordomas with a predominant cartilaginous differentiation had a much better prognosis. Subsequent studies have suggested that this difference in prognosis is not true. Some studies have suggested that younger patients have a better prognosis than older patients. Chordomas were typically stained with keratin. Some studies have suggested that chondroid chordomas do not stain with keratin, and hence, consider these to be chondrosarcomas. My approach is to make a diagnosis of chondroid chordoma if roentgenographic features suggest that the lesion involves the clivus and the biopsy shown cartilage.

Some chordomas undergo dedifferentiation into a high grade spindle cell sarcoma either after radiation or with recurrence. These tumors are associated with a bad prognosis.
Major advances have been made in the treatment of chordomas along the spinal column and the sacrum. It has been recognized that if the lesion can be resected without contaminating the area, the prognosis is excellent. Chordoma is a locally aggressive tumor with little potential for metastasis. Mortality is usually associated with uncontrolled local recurrence. Even with involvement of vertebral bodies, resectional surgery can be performed. No resectional surgery, of course, is possible with chordoma of the base of the skull. Many patients have benefited from radiation therapy in this location.
REFERENCES


CASE 15 - ACCESSION 23018

GIANT CELL TUMOR
Giant cell tumors comprise approximately 23 percent of all benign tumors in the Mayo Clinic files. Giant cell tumors are one of the few neoplasms of bone in which there is a definite female predilection. Over 55 percent of patients with giant cell tumor in the Mayo Clinic files were women. This predominance was even more striking when considering patients in the first two decades of life. The majority of patients with giant cell tumor are over 19 years of age with the peak incidence being in the third decade of life. There were only three patients in the first decade of life, and only 10 percent were over the age of 50.

Most giant cell tumors are found at the end (epiphyses) of long bones. Almost half of all tumors occur around the knee joint involving the distal femur and the proximal tibia. The distal end of the radius is the third most common location for a giant cell tumor. This is a most unusual location for any other kind of bone lesion. A young woman presenting with a purely lytic destructive lesion of the radius almost surely will have a benign giant cell tumor. The sacrum is the fourth most common location for giant cell tumors. However, the vertebrae above the level of the sacrum are uncommonly involved. If they do occur in the vertebrae, they involve the body of the vertebrae. Aneurysmal bone cysts, in contrast, involve the posterior elements. The small bones of the hands and feet are rarely involved. Most giant cells containing lesions of these small bones will be a variant. Almost all giant cell tumors involve the epiphysis. There were only six giant cell tumors involving the metaphysis in the Mayo Clinic files.

Pain of variable severity is almost always the symptom. Patients may also complain of swelling. A hard, sometimes crepitant, painful mass may be palpated.
Roentgenograms show a purely lytic lesion involving the end of the bone. The patients are usually mature, and hence, the epiphyseal plates are closed. The lesion should extend to the articular cartilage or close to it. It usually involves the bone in an eccentric fashion, may destroy the cortex, and form a soft tissue mass. The margins may be well defined or poorly demarcated. Sclerosis is unusual around a giant cell tumor. Sclerosis within the lesion is very unusual in a giant cell tumor. However, when it extends into the soft tissue, the rim of sclerosis is usually present demarcating the tumor from the soft tissue. When the lesion recurs in the soft tissue, it very characteristically has a rim of calcification reminiscent of an eggshell.

Grossly, a giant cell tumor has a very characteristic dark brown color. Areas of necrosis may be seen. Frequently areas of yellow discoloration are found. The lesion may be partly or predominantly cystic.

Giant cell tumors show proliferation of mononuclear cells and giant cells. The giant cells may contain from 40 to 60 nuclei and are distributed more or less uniformly throughout the lesion. The mononuclear cells have round to oval nuclei which resemble the nuclei of those seen in the giant cells. Mitotic figures may be prominent in the mononuclear cells. However, they do not show cytological atypia. Vascular invasion may be seen at the edge of the lesion. Some giant cell tumors will show spindle cell areas with a storiform pattern. This may suggest a diagnosis of a fibrohistiocytic neoplasm. If a biopsy from the end of the long bone shows features of a benign fibrous histiocytoma, a diagnosis of giant cell tumor should be entertained. Some giant cell tumors will contain large numbers of foam cells. Occasionally one may find areas of new bone formation within an otherwise typical giant cell tumor. Cystic areas are commonly found in giant cell tumors. Secondary aneurysmal bone cysts are not unusual at least
in foci. Occasionally the cystic spaces predominate, and the giant cell tumor may be present as a mural nodule. Histologic grading of giant cell tumors has no prognostic significance.

Giant cell tumors are ordinarily treated with curettage and bone grafting. In the past, 50 percent recurrence rate was accepted. With more modern techniques, one can expect a recurrence rate of 25 percent. Radiation should be implied only if surgical options are not viable.

A small percentage of patients will develop pulmonary metastasis even though the cytologic features suggest a benign neoplasm. Most of these patients have a solitary focus of metastasis, and once the lesion is removed, the patient is cured. However, there have been well-documented examples of patients getting incurable metastasis and dying from giant cell tumor of bone. On the other hand, there are examples of patients with multiple metastasis in the lung, either remaining stable or regressing.

The diagnosis of malignant giant cell tumor is tenable only if a benign giant cell tumor can be demonstrated either in the past or at the time of a biopsy. Most patients with malignancy arising in giant cell tumor have had a giant cell tumor treated in the past with radiation. Hence, these tumors can be considered to be post-irradiation sarcoma. Rarely one gets a high grade sarcoma at the site of a giant cell tumor which has only been previously treated surgically. Rarely one will find a lesion with all the clinical features of a giant cell tumor but with a high grade malignancy juxtaposed to a typical giant cell tumor.
REFERENCES


CASE 16 - ACCESSION 27810

METASTATIC CARCINOMA
Metastatic carcinoma is by far the most common malignant tumor of bone. Metastatic carcinoma usually does not give rise to diagnostic problems. The patient is known to have a type of malignancy, and a bone biopsy may be done just to confirm the presence of metastasis. However, diagnostic problems may arise when metastasis to the bone is the first manifestation of a malignant process.

Most patients with metastatic malignancies are older adults. Metastatic malignancies may be seen in the very young age group also with metastatic neuroblastoma and other renal cell malignancies. It is unusual to see a metastatic malignancy in the young patient who usually gets primary bone neoplasms.

Patients usually complain of localized bone pain. A pathologic fracture may be the presenting symptom of a metastatic carcinoma.

Metastatic tumors usually produce irregular destruction of bone indicating a malignant process. Most metastatic carcinomas are lytic, although some metastatic carcinomas notably for the prostate can be osteoblastic. A purely lytic destructive lesion which may have an aneurysmal dilatation strongly suggests metastatic hypernephroma.

Radioactive bone scans may show involvement of multiple skeletal sites. Magnetic resonance imaging may be helpful in the vertebrae.

Carcinomas metastatic to bone do not have gross diagnostic characteristics. The lesions may be soft and fleshy to firm and even bony.

The diagnosis of metastatic carcinoma is almost always easy. The presence of epithelial cells in a bone biopsy is diagnostic of carcinoma. The most common carcinomas which metastasize to the bone in my experience are breast, prostate, lung, and kidney. It is unusual to see a metastatic
thyroid carcinoma in the skeleton in the absence of an obvious thyroid primary.

Oncologists usually like to know the primary site of the metastatic carcinoma when it is not obvious clinically. Some metastatic carcinomas have obvious histologic characteristics suggesting their origin. Metastatic thyroid carcinoma with production of colloid and metastatic hepatoma with the production of bile are obvious examples. However, metastatic high grade adenocarcinoma may not suggest a specific source. However, the pathologists may be able to direct the clinician in the search for the primary sites. Immunoperoxidase stains such as those for prostate carcinoma may be helpful. This is of more than academic interest because some metastatic carcinomas are amenable to hormonal manipulation.

Metastatic sarcomatoid carcinoma can still present diagnostic difficulties. In my experience the most common site for such a metastasis is a hypernephroma. Many hypernephromas do not stain for keratin. Most metastatic sarcomatoid carcinomas have plump spindle cells whereas fibrosarcomas, which stain very similarly, have usually slender spindle cells. Sampling of the biopsy may show obvious hypernephroma areas. It is important to keep the possibility of a metastatic sarcomatoid carcinoma in mind when diagnosing a fibrosarcoma in an older adult. The clinician should rule out the possibility of an occult primary site before definitive surgical treatment. Even then an occasional mistake is bound to be made.

The treatment of metastatic carcinoma has undergone great changes. In the past no treatment was attempted. Orthopedic oncologists treat metastatic carcinoma aggressively if there is a pathological fracture or if there is a threat of a pathological fracture. Hence, resected specimens of
bones with metastatic carcinoma are commonly seen in the lab. Many carcinomas, especially those from the breast and the prostate, may respond to hormonal manipulation.

The prognosis in metastatic carcinoma depends upon the site and the clinical situation. Patients who present with metastatic carcinoma do very poorly. However, patients with a known hypernephroma who have already been treated for the primary tumor may have a prolonged survival even with a bony metastasis. Patients with prostate and breast cancer also may survive for a long time after bony metastasis. On the other hand, patients with a carcinoma of the lung and skeletal metastasis have a very poor prognosis.
REFERENCES

CASE 17 - ACCESSION 27764
ANEURYSMAL BONE CYST
A variety of cystic lesions can involve the skeleton. They may simulate a neoplasm. Aneurysmal bone cyst is by far the most common of these cystic lesions.

Aneurysmal bone cysts are just about half as frequent as a giant cell tumor. Aneurysmal bone cysts show a slight predilection for females. About 80 percent of patients with aneurysmal bone cysts will be in the first two decades of life. However, aneurysmal bone cysts may be seen in older individuals also. In the Mayo Clinic files, the oldest patient with an aneurysmal bone cyst was 65.

The region around the knee including the distal femur and the proximal tibia is the most common site for aneurysmal bone cysts. However, any portion of the skeleton may be involved. The spine is rather frequently involved. The cervical portion of the spine is the most common site. When aneurysmal bone cysts involve the vertebrae, they tend to involve the posterior elements. Giant cell tumors, on the other hand, involve the body.

Pain and swelling are the most common complaints. Rarely a pathological fracture will be the presenting symptom. Patients with involvement of the vertebrae may show neurological symptoms. Physical examination may reveal a mass lesion.

A typical roentgenographic appearance of an aneurysmal bone cyst is an area of lucency situated eccentrically in the medullary cavity in the metaphysis of the long bone. Less commonly the lesion is situated centrally in the medullary cavity. Rarely the lesion may appear to arise in the cortex or in the periosteum. Very characteristically the lesion destroys the cortex and bulges into the soft tissue. The soft tissue extension is well demarcated and may be surrounded by a rim of sclerosis. The margins may be well
defined or poorly defined. In a small number of cases, the roentgenographic features may suggest a malignant neoplasm. CT scans usually show fluid levels which are practically diagnostic of an aneurysmal bone cyst. Magnetic resonance images show a honeycomb appearance highlighting the spaces and the septa.

Most often the gross specimen is received in fragments. The tissue is in the form of red granular material. Occasional foci of calcification may be seen. One characteristic aspect is that the gross specimen is considerably smaller than would be expected from the roentgenographic appearance. If the lesion is resected intact, spaces separated by thin walled septa are found.

On low power, aneurysmal bone cysts have the appearance of spaces separated by septa. The lining of the septa usually contains a thin rim of osteoid which has been termed "fiber osteoid." The septa show a large number of capillaries. There is a loose arrangement of spindle cells within the septa. Giant cells are almost always found. Mitotic figures may be prominent, but cytological atypia is absent. Most aneurysmal bone cysts will have some relatively solid areas. These areas show a loose arrangement of spindle cells usually with reactive new bone formation. This new bone is in the form of osteoid or bony trabeculae with prominent osteoblastic activity. The pattern of bone production is that seen in a reactive process and not a neoplasm. Very typically peculiar blue areas of calcification are seen in the stroma. Some aneurysmal bone cysts will have relatively solid areas. Indeed, some aneurysmal bone cysts will appear completely solid grossly and microscopically. These areas are composed of loosely-arranged spindle cell proliferation and usually reactive new bone formation.

The differential diagnosis involves giant cell tumor and osteosarcoma. Giant cell tumors occur at the ends of bone in patients with mature skeleton.
Aneurysmal bone cysts occur in the metaphysis of skeletally immature patients. Aneurysmal bone cyst-like areas may be seen in a giant cell tumor. However, typical areas of a giant cell tumor should not be seen in an aneurysmal bone cyst. Telangiectatic osteosarcoma is also in the differential diagnosis. The clinical roentgenographic and gross features may be identical between these two lesions. However, in telangiectatic osteosarcoma, the septa are lined with very pleomorphic nuclei whereas in aneurysmal bone cysts they do not show any cytological atypia. A solid aneurysmal bone cyst may be mistaken for a low grade osteosarcoma. Low grade osteosarcoma is much less cellular than an aneurysmal bone cyst, and the pattern of bone production is not that of a reactive process.

Treatment is surgical removal. Recurrences may develop, but even they can be managed conservatively. The prognosis is excellent. Spontaneous malignant change has not been seen in the Mayo Clinic files. However, there has been one case report in the literature.
REFERENCES


CASE 18 - ACCESSION 25801

FIBROUS DYSPLASIA
Fibrous dysplasia is probably the result of an aberration in the development of bone. It may be solitary or multifocal. When, in addition to polyostotic fibrous dysplasia, the patient shows cutaneous pigmentation and endocrine abnormalities such as precocious puberty in girls, the condition is commonly called Albright's syndrome.

The true incidence of fibrous dysplasia is unknown. Many patients are asymptomatic and, hence, may not come to clinical attention. There were approximately 550 examples of fibrous dysplasia in the Mayo Clinic files until the end of 1993. There is a slight female predominance. Most patients with fibrous dysplasia are in the second and third decades of life. However, patients with fibrous dysplasia of the rib tend to be older. This probably results from the fact that these lesions are asymptomatic and are incidental findings found when chest x-rays are taken for some other reasons in older individuals.

Any portion of the skeleton may be involved with fibrous dysplasia. However, there are some distinct sites of predilection which may be divided as follows: (1) jaw bones, (2) skull, (3) ribs, and (4) the rest of the skeleton. Among the long bones, the proximal femur is the most common site. The maxilla is much more likely to be involved than the mandible.

As mentioned previously, many lesions of fibrous dysplasia are asymptomatic. Patients with involvement of the jawbones present with deforming swellings. Fibrous dysplasia of the proximal femur may cause a pathological fracture. Patients with involvement of the skull and jawbones may show swelling. Patients with polyostotic fibrous dysplasia may show skin pigmentation.

Roentgenograms show well-defined zones of rarefaction. This area of rarefaction is surrounded by a narrow rim of sclerotic bone. Occasionally
the lesion will produce a large expansile mass especially in the ribs. Some examples of fibrous dysplasia will contain a large amount of bone and, hence, may be relatively radio-opaque. Some examples of fibrous dysplasia will show calcification typically seen in cartilaginous lesions. Rarely an example of fibrous dysplasia will show a destructive area which represents a secondary aneurysmal bone cyst.

Grossly, fibrous dysplasia presents as white firm tissue which may feel gritty because of the presence of bony fragments. Cystic change, yellow areas representing collections of foam cells, and islands of cartilage may also be present.

The histological feature is that of proliferation of plump fibroblasts that produce dense cartilaginous matrix. The cells tend to be plump and short and not elongated as seen in sarcomas. Mitotic figures are extremely uncommon. Bony trabeculae of unusual shapes are present within this fibrous proliferation. These bony trabeculae lack the arrangement usually seen in medullary bone. They sometimes have the appearance of the letter "C." Typically, osteoblastic rimming is absent around these bony trabeculae. However, the presence of osteoblastic activity does not rule out the diagnosis of fibrous dysplasia. Occasionally the bony trabeculae are in the shape of round ossicles which may appear psammomatous. Collections of foam cells are commonly found in fibrous dysplasia. In limited biopsy material, this may be mistaken for a clear cell carcinoma. Some examples of fibrous dysplasia will show large islands of cartilage. These cartilaginous nodules do not show any cytological atypia. Some fibrous dysplasias will show large areas of myxoid change in the matrix which may make diagnosis difficult.
The treatment of fibrous dysplasia is surgical. An incidental asymptomatic lesion need not be treated. Most lesions of the jawbones are treated so as to reduce deformities.

Osteofibrous dysplasia is a form of fibrous dysplasia which was first described by Dr. Campanacci from Italy. This typically involves the tibia and occasionally the fibula in young children. The lesion is cortical whereas lesions of fibrous dysplasia are medullary. Roentgenograms show multiple lucencies within the cortex with sclerosis surrounding them. This roentgenographic appearance is very similar to that seen in adamantinoma. Microscopically there is fibroblastic proliferation with benign giant cells and osteoid trabeculae. These bony trabeculae are usually rimmed with very prominent osteoblasts. The similarity between osteofibrous dysplasia and adamantinoma on x-ray has suggested that there may be the relationship between the two. Several immunoperoxidase studies have shown that examples of osteofibrous dysplasia will frequently show keratin-positive cells. This has led some authors to believe that osteofibrous dysplasia represents a regressed form of adamantinoma. Other authors believe that osteofibrous dysplasia may develop into adamantinoma. I believe that there is a resemblance at least roentgenographically between osteofibrous dysplasia and adamantinomas. However, I do not believe they are otherwise related.
REFERENCES


CASE 19 - ACCESSION 27808

HISTIOCYTOSIS X
Histiocytosis X or Langerhans' cell's histiocytosis is a disease of unknown etiology with variable clinical manifestation. It may present as a solitary lesion in bone, be a chronic disseminated form, or may present as an acute fulminant disease. The chronic disseminated form has the classic triad of exophthalmos, diabetes insipidus, and multiple bone lesions. This has been referred to as Hand-Schüller-Christian disease. The acute disseminated form with involvement of the skin, hepatosplenomegaly, and bone disease has been referred to as Letterer-Siwe syndrome. There is controversy in the literature concerning Letterer-Siwe syndrome. Some authors believe that Letterer-Siwe syndrome does not belong in the group of histiocytosis X. It is possible that several different conditions such as leukemic infiltrates can give rise to the syndrome. However, I do believe that at least some examples of Letterer-Siwe disease result from proliferation of the typical histiocytes.

Dr. Kilpatrick has recently reviewed our material of skeletal histiocytosis X. There were 263 patients with histiocytosis X. There were 172 patients below the age of 17 and 91 patients who were considered to be adults. Although the majority of patients with histiocytosis X will be children, it is by no means uncommon in adults. The oldest patient was 71 years old. Males predominated by a ratio of 1.6:1 in both adults and children. Most patients presented with pain. Some patients complained of pain which is worse at night awakening them from sleep. This lead to a preoperative diagnosis of an osteoid osteoma in one patient. Patients with involvement of the jawbones characteristically complained of loose teeth.

The most frequent sites of involvement were the skull, the femur, the jaw, the pelvis, and the spine. The ribs tended to be more commonly involved in adults. The posterior portions of the jawbones were most
commonly affected. Exophthalmos was seen in 19 pediatric patients and 1 adult. Forty patients had symptoms of diabetes insipidus. Crusting eczema or seborrhea-like rash was reported in 13 percent of children and 4 percent of adults. Eight patients had hepatosplenomegaly. There were 19 patients who showed involvement of the lung.

Roentgenograms show solitary or multiple sites of involvement in the skeleton. The roentgenograms generally show purely lytic lesions which are well circumscribed. Histiocytosis X usually produces periosteal new bone formation. The periosteal new bone usually has multiple thick layers suggesting a benign indolent process. When histiocytosis X involves a flat bone, it may have a destructive appearance suggesting a malignant neoplasm. Involvement of the vertebral body usually gives rise to collapse of the vertebral body giving rise to what has been called vertebrae plana.

The dominant histological feature of histiocytosis X is a proliferation of very characteristic histiocytes. These cells are usually in clusters and do not form tight sheets. The cells have well-defined cytoplasmic boundaries and oval-shaped nuclei with longitudinal grooves. Occasionally the cells have rounded nuclei and abundant pink cytoplasm giving rise to an epithelioid appearance. Mitotic figures may be abundant. Very typically the histiocytes are associated with eosinophils. Occasionally the eosinophils form sheets and undergo necrosis to give rise to eosinophilic abscess. Other inflammatory cells such as lymphocytes and neutrophils are also commonly present. Areas of necrosis are commonly found in histiocytosis X of bone. There is no difference in the histology between lesions which are unifocal and those which are multicentric. The cells of histiocytosis X stain positively with the S100 protein. Electron microscopy shows very characteristic cytoplasmic inclusions called bierbeck granules.
The prognosis in patients with solitary bone involvement is excellent. Rarely a patient with a solitary bone lesion will develop disseminated disease and even die of the disease. Patients who present with disseminated disease especially hepatosplenomegaly are more likely to die of disease. Involvement of the skeleton only is usually associated with an excellent prognosis.
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CASE 20 - ACCESSION 27809

BIZARRE PAROSTEAL OSTEOCHONDROMATOUS PROLIFERATION
Bizarre parosteal osteochondromatous proliferation of bone was first described in 1983 by Nora and co-authors. They described an unusual proliferative lesion involving the small bones of the hands and less often of the feet. The lesions resemble osteochondromas.

Meneses and co-authors recently described 65 examples of Nora's disease. There were slightly more females than males, and the patient's age ranged from 8 to 73 years. About three-fourths of the lesions involve small bones of the hands and feet. The remainder showed involvement of the long bones. More than half of all the lesions involved the small bones of the hands. Patients usually complained of a mass formation. Pain was unusual.

Roentgenograms show a well-marginated mass of mineral arising from the cortical surface of the affected bone. The underlying bone shows little or no alteration. The lesion is attached to the cortex but shows no continuity with the underlying medullary canal.

Grossly the lesions measured from 1/2 to 3 cm in greatest dimension. Histologically, Nora's disease shows three different components: cartilaginous proliferation, bone formation, and spindle cell formation. The cartilage is usually in the form of a cap or may be arranged in lobules. The chondrocytes are in lacunae and may have prominent nuclei. The hypercellularity and prominent cytological changes may suggest a diagnosis of chondrosarcoma. The nodules of cartilage, however, mature into trabecular-appearing bone. At the junction between the cartilaginous cap and the underlying bone, there is a very distinctive blue tinctorial quality. The bony trabeculae are separated by a loosely arranged spindle cell proliferation.

The differential diagnosis involves chondrosarcoma, osteosarcoma, osteochondroma, and parosteal osteosarcoma. Osteochondromas are
extremely uncommon in the small bones of the hands and feet. In the long bone, lack of continuity between the medullary cavity and the lesion on x-ray rules out the possibility of an osteochondroma. Histologically in an osteochondroma, one sees fatty or hematopoietic marrow between the bony trabeculae whereas in Nora's lesion there is spindle cell proliferation. The presence of hypocellular proliferating cartilage may suggest a diagnosis of a chondrosarcoma. However, chondrosarcomas made of hyaline cartilage are extremely uncommon in soft tissues anywhere. The fact that the lesion tends to undergo maturation into trabecular-appearing bone also should suggest that this is a reactive process rather than a neoplasm. Parosteal osteosarcomas may show cartilage in the form of a cap. Spindle cell proliferation between bony trabeculae is also seen in parosteal osteosarcoma. However, in parosteal osteosarcoma the spindle cells are not loosely arranged but show dense collagen between them. In Nora's lesion the spindle cells show a loose arrangement as seen in other reactive processes.

Bizarre parosteal osteochondromatous proliferation is a form of myositis ossificans. It may recur just as myositis may. In fact, in the patients in whom follow-up information was available, over 50 percent have had one or more recurrences. However, none of these lesions behaved in a malignant fashion.
REFERENCES
