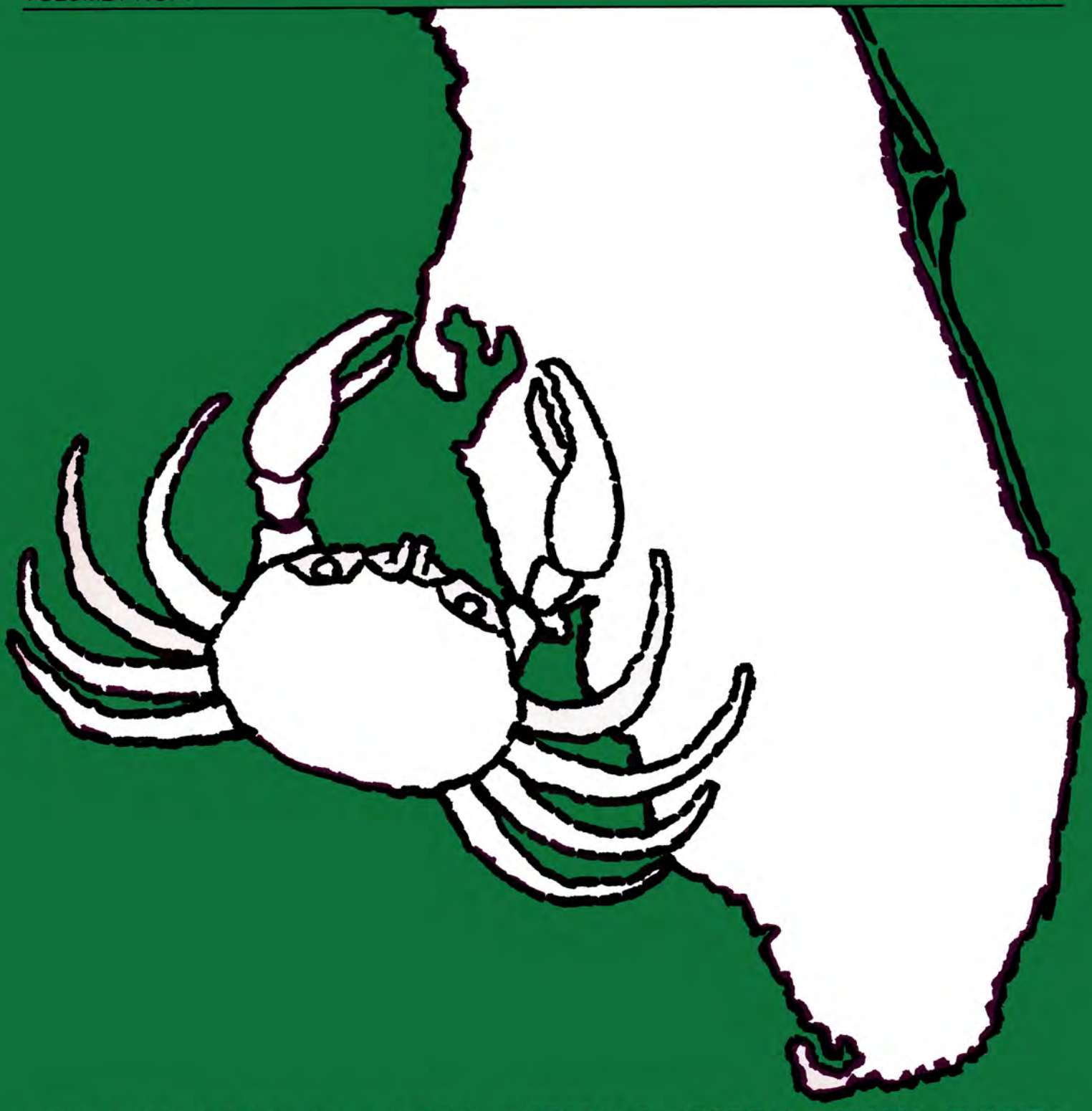
cancer seminar

VOLUME I NO. 1 SECOND SERIES



UNIVERSITY OF SOUTH FLORIDA • VETERANS HOSPITAL • TAMPA, FLORIDA

CANCER SEMINAR

SECOND SERIES, VOLUME ONE AUGUST, 1976 NUMBER ONE

Juan A. del Regato, Editor

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BONE TUMORS

For a quarter of a century, from 1949 to 1973, these CANCER SEMINARS were held annually in Colorado Springs. Through the initiative of Dr. Arthur Graham, Professor and Chairman of the Department of Radiology, this second series of CANCER SEMINARS was initiated under the auspices of the University of South Florida College of Medicine and the U.S. Veterans Administration Hospital of Tampa, Florida.

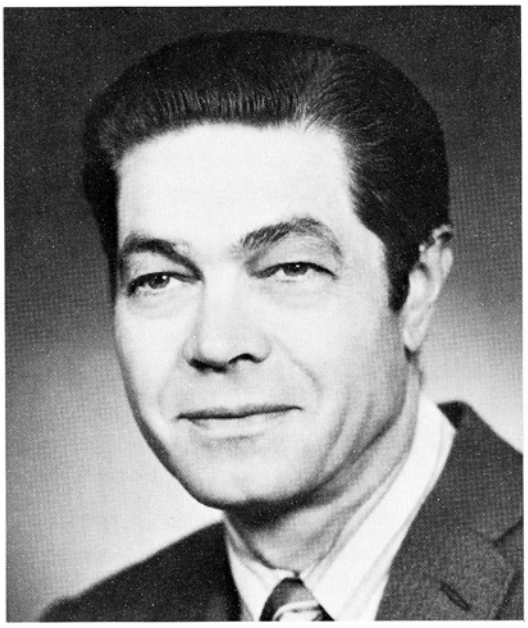
CANCER SEMINAR is basically a confrontation of the clinical, radiodiagnostic and histopathologic data in a chosen number of problem cases. The discussion provides an opportunity for therapeutic and prognostic considerations. For this first CANCER SEMINAR, the subject of bone tumors was chosen; with the help of Dr. Henry Azar, Professor of Pathology and Chief of Lab, V. A. Hospital, 15 cases were selected from those proposed. Clinical summaries and carefully made (LogEtronic) reproductions of the roentgenograms were sent to participating radiologists in this country and abroad. A set of 15 carefully prepared histopathologic slides were mailed to participating pathologists. The gathered opinions of radiologists and pathologists were tabulated in advance of the seminar.

On March 15th, 1975 we gathered at a hotel in St. Petersburg, Florida. Invited as guests for the occasion were: **Dr. Philip J. Hodes,** former Professor of Radiology at the University of Pennsylvania and Jefferson Medical College and presently at the University of Miami, Florida. Dr. Hodes is a recognized teacher and authority in the radiodiagnosis of bone tumors. **Dr. David C. Dahlin,** Professor of Pathology at the Mayo Foundation of Rochester, and author of a book on the pathology of bone tumors, was the guest pathologist. Opening the discussion of every case was **Dr. Franklin J. Sims,** a worthy representative of the new generation of orthopedic surgeons, of the Department of Surgery at Mayo Clinic. The discussions were enriched by the contributed comments of participants and by the experience of those in attendance.

CANCER SEMINAR requires considerably greater preparation and work than it may appear. We owe special thanks to Mr. Walter McAllister and to his dedicated histopathology associates for the preparation of over 6,000 slides required for the CANCER SEMINAR. The good quality of the photomicrographs which appear with the text are due to the personal attention given by Dr. Azar and to the workers of the Department of Medical Media Production of the Veterans Administration Hospital. In the preparation of the manuscript for publication, we have received the support of the secretaries in the Department of Radiology, as well as of my office.

The publication of CANCER SEMINAR has been made possible by a generous grant of the MILHEIM FOUNDATION for Cancer Research, of Denver; this grant is to be used as a revolving fund for the publication of this and future proceedings. We are truly thankful.

J. A. del Regato, M.D.
Tampa, Florida
Sept. 1976

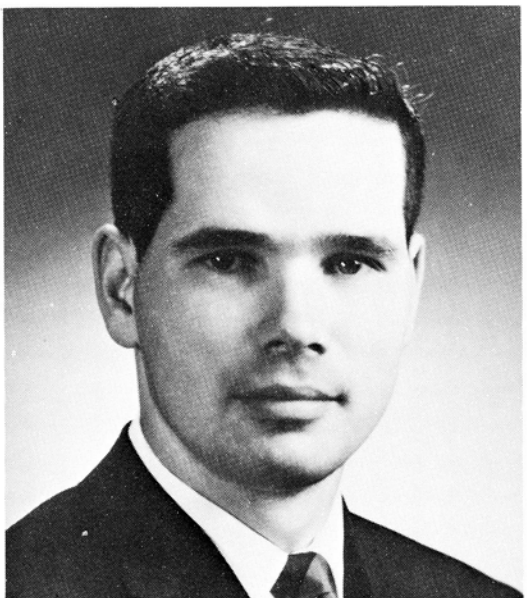


DAVID C. DAHLIN, M.D.

Professor of Pathology, Mayo Foundation, Rochester, Minnesota. Dr. Dahlin is author of a well known authoritative book on pathology of bone tumors.

PHILIP J. HODES, M.D.

Professor of Radiology, University of Miami Medical School and Chief of the Department of Radiology at Jackson Memorial Hospital. Dr. Hodes is former Professor of Radiology at the University of Pennsylvania and of the Jefferson Medical College of Philadelphia.



FRANKLIN H. SIM, M.D.

Orthopedic surgeon on the staff of the Mayo Clinic and member of the Department of Surgery, Mayo Foundation, Rochester, Minnesota.

1. Non-Caseating Granuloma (Sarcoidosis) of Lungs and Ribs

Contributed by **H. Cherin, M.D.** and **H. Azar, M.D.**, Tampa, Florida

The patient was a young man, 25 years of age, in February 1974, when he gave a history of bilateral flank pains of five months duration; there had been a 20 lbs weight loss and he had experienced night sweats, malaise and occasional fever. On examination there was tenderness to palpation of the 7th and 8th left ribs and small, tender, left axillary adenopathy. The serum glucose, chlorides, sodium and potassium were all within normal limits; the electrophoresis showed non-specific increase in gamma globulins.

Dr. Hodes: The following clinical features which include weight loss, night sweats and fever in a twenty-five year old young man suggest a granulomatous or lymphmatous process.

The films of the chest reveal bilateral hilar adenopathy which could be explained by the aforementioned clinical possibilities. I believe the very heart of the case, however, relates to the bone changes.

I am excluding a lymphomatous process because of the nature of the rib lesions. Lymphomatous rib lesions are usually more destructive or reactive. Usually one does not find expansile cystic lesions associated with perifocal bone reaction in lymphoma.

The cystic nature of this rib lesion and its perifocal reactive change makes one think of osteitis tuberculosa multiplex cystica. This would also account for the mediastinal lymph nodes which could be tuberculous. However, cystic tuberculosis is a process which occurs earlier in childhood and not at the age of twenty-five. Because of this one must bring a closely related entity into focus, sarcoid.

Usually the small bones of the hands and feet are involved in sarcoid. The involvement is the result of the perivascular infiltration of the Haversian canals with thinning of the cortex plus destruction of the fine trabeculae within the bone marrow. Commonly these bone lesions are not associated with clinical complaints. The lesions often spontaneously regress but sometimes fibrous tissue, the result of the healing process, persists with the formation of residual cyst-like lesions of the type in this rib.

Fig. 1—Bilateral hilar adenopathy.

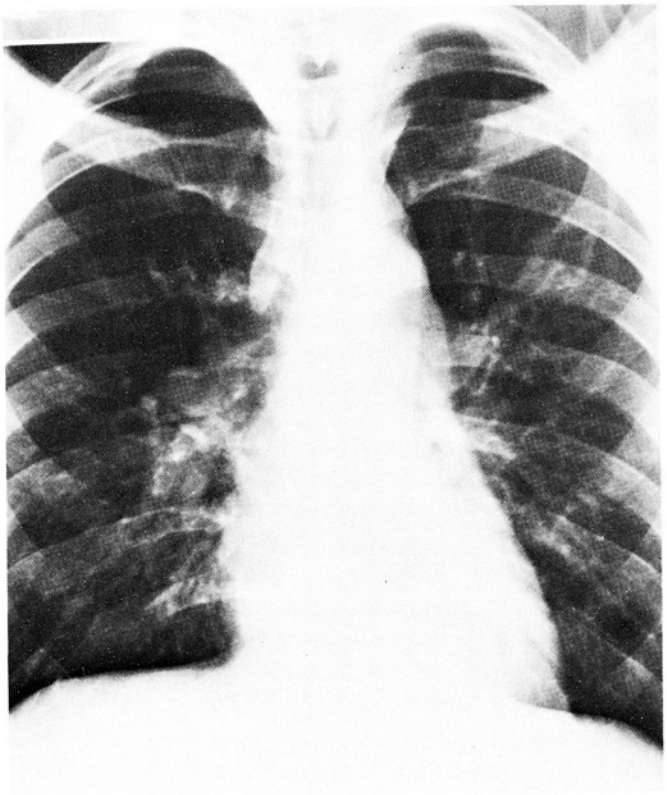
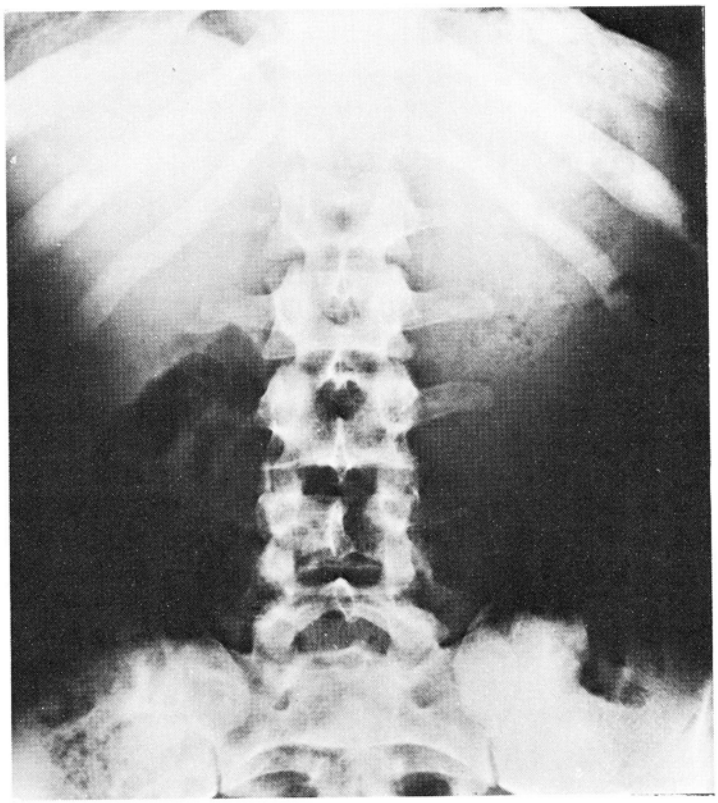


Fig. 2—Lytic lesions of the ribs.



Dr. Hodes' Impression: Sarcoid.

Radiologic impressions submitted:

Hodgkin's disease	50
Malignant "lymphoma"	49
Sarcoidosis	07
Metastatic tumors	06
Tuberculosis	06
Granuloma	04
Myeloma	03
Others	24

Dr. Hodes: On the basis of the mediastinal lesion one would consider Hodgkin's or lymphosarcoma, but I don't believe the bone lesions are compatible: they are sharply demarcated, well-circumscribed. I am glad to see that a few agreed with the diagnosis of sarcoid. A metastatic tumor that would give the bone lesions would not produce the hilar adenopathy. Tuberculosis perhaps. Myeloma at age 25, no way!

Dr. del Regato: Dr. John Madewell, of the Armed Forces Institute of Pathology, Washington, D.C., on the basis of the roentgenogram of the chest and the lytic lesions of the ribs with sclerotic rim, suggested tuberculosis. Dr. James B. Dennis, of Ann Arbor, preferred aspergillosis. Drs. R. D. Bretz, of Long Beach, California and L. Bigongiari, of Ann Arbor, offered Hodgkin's disease. Dr. R. L. Washburn, of Ann Arbor, preferred myeloma; Dr. M. Valette, of Creteil, France, and Drs. G. Lodwick and C. Farrell, of Columbia, Missouri, offered sarcoidosis.

The University of Missouri radiodiagnostic computer was unable to diagnose this case of multiple lesions. When consulted about only one lesion, it answered: chondromyxoid fibroma.

Operative findings: On April 3rd, 1974, a segmental sub-periosteal rib resection was done for histologic study. A segment of rib 6.5 x 2 cm was removed which contained an ovoid shaped gray-white irregular area with loss of cortical bone and periosteum.

Dr. Dahlin: Microscopically one sees what appears to be a total cross section of a small bone, probably the rib. Approximately one-half of its substance is replaced by granulomatous inflammatory tissue which has penetrated through the cortex and invaded the adjacent soft tissues. The inflammatory mass is granulomatous in that the individual inflammatory subunits are surrounded by a fairly well palisaded zone of epitheliod cells. Necrosis is present in the centers of a few of these granulomas. Special stains for fungi and for acid fast organisms do not reveal any identifiable organisms. In our own laboratory we would assume that such a granulomatous lesion in bone is due to some specific microorganism and would depend on microbiologic investigation for determination of the type of organism. The lesion shows no evidence of neoplasm.

The differential diagnosis must include a lesion of sarcoidosis but the granulomatous centers of the lobules and the rather aggressive clinical behavior of the lesions in this case make that diagnosis unlikely. Tuberculosis is probably highest on the list of probabilities because no organisms can be identified. Any of the systemic mycotic infections could produce this histologic pattern but they would be apt to contain recognizable organisms.

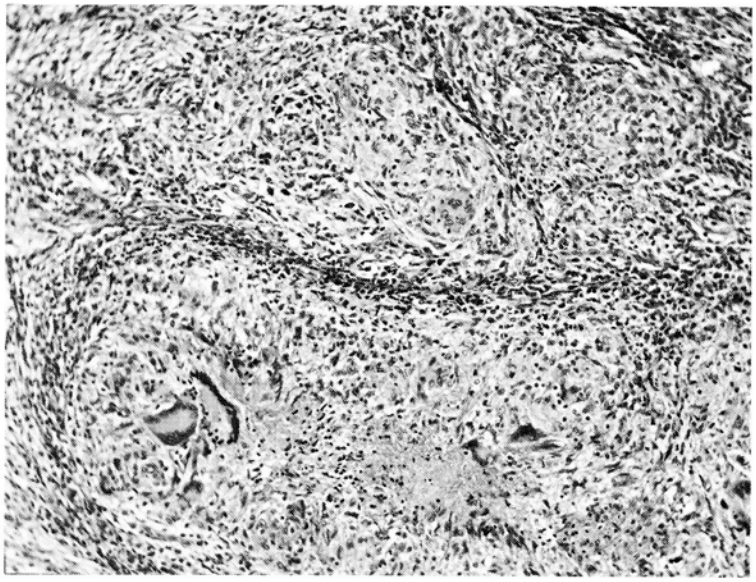


Fig. 3—Granulomatous tissue with surrounding palisaded zones of epithelioid cells (x 160).

Dr. Dahlin's diagnosis: GRANULOMA, probably specific.

Histopathologic diagnoses submitted:

Tuberculosis	46
Chronic granuloma	31
Mycosis (Blasto, coccidio, histo)	30
Sarcoidosis	13
Osteomyelitis	09
Others	05

Dr. Dahlin: I don't think that the diagnosis of tuberculosis demands further comment. Chronic granuloma is probably a safer thing to call it. Sarcoidosis we would rule out to some degree because necrosis should not be present, but if every test is negative, such diagnosis would have to be accepted, by exclusion. A diagnosis of osteomyelitis should not be considered because of the granuloma.

Dr. del Regato: Drs. McGavran, of Hershey, Pennsylvania and Leo Lowbeer, of Tulsa, Oklahoma, made a diagnosis of caseating granulomatous osteomyelitis probably due to tuberculosis. Dr. H. A. Sissons, of London, made a diagnosis of tuberculosis; he commented that the absence of bone necrosis is unusual in tuberculosis but the presence of necrosis in the follicular lesions suggests that the lesion is not sarcoidosis.

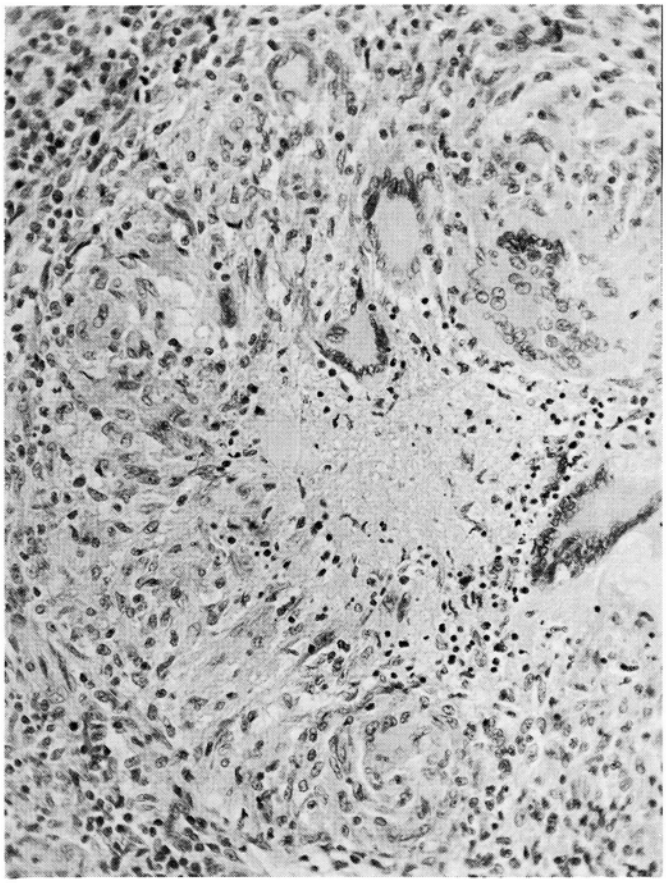
Dr. N. N. Hadders, of Gronningen, Holland and Dr. F. Cabanne, of Dijon, France suggested a North American blastomycosis.

Dr. Lent C. Johnson, of the AFIP in Washington, D.C., wrote: This granuloma has a high probability of being tuberculous . . . a possibility of being fungal . . . and even a slight possibility of being spirochetal in origin. It is not sarcoid.

Subsequent history: The acid fast stains were negative; fluorescent stains and stains for fungi were non-contributory. Since 1974 the patient has been receiving prednisone every other day; he gained weight at first but has now stabilized his weight; he feels well and has no complaints. On February 28, 1975, he was engaged in studies to become a minister of the gospel.

Dr. Sim: In this patient with pulmonary disease and multiple osseous lytic lesions associated with systemic manifestations, one must suspect tuberculosis or other granulomatous diseases of bone including brucella, fungal diseases and sarcoidosis. Before we would decide on an open biopsy of a rib, a great deal is to be done clinically in the way of radiographic surveys, skin testing, scans, bronchial and gastric washings and urine cultures. Efforts must be made not only to determine the etiology of the lesion but to determine the extent of the disease. On the basis of the available biopsy, a caseating granulomatous lesion found pathologically should be dealt with as tuberculosis at least initially. It takes 6-8 weeks for bacteriological confirmation and during this period the patient should be put on chemotherapy. There is an increased awareness of microbacterial infections other than those caused by microbacterium tuberculosis. Careful clinical and bacteriological distinction between these different diseases is important, for proper selection of therapeutic aids is necessary in atypical microbacteria. Probably the agent of choice would be Ethambutol as this would cover both tuberculosis and atypical tuberculosis. Sarcoidosis is a possibility. Seventeen percent of patients with sarcoidosis have manifestations primarily involving the peripheral bones. After the initial period of drug treatment, if the cultures were negative, then treatment for sarcoidosis is indicated. The clinical course of sarcoidosis is unpredictable. Prednisone therapy may minimize the dissemination and progression.

Fig. 4—Inflammatory tissues surrounding necrosis (x 250).



Dr. Henry Azar, Tampa, Fla.: I would like to comment on Dr. Dahlin's diagnostic conclusions. One may have observed, indeed, microfoci of necrosis in granulomas of all types, including sarcoidosis. One reaches a diagnosis of sarcoidosis with reluctance, not only on the basis of identifiable etiology and of histology, but after taking into consideration the clinical behavior of the patient. This patient had a tuberculin negative reaction. In spite of his disseminated disease, he was comfortable even after prolonged treatment with prednisone. I think all of these factors should be taken into consideration. My diagnosis is non-caseating granuloma, compatible with sarcoidosis - sarcoidosis being a disease complex and not a specific lesion.

Dr. del Regato: Thank you Dr. Azar. Dr. Henry Garland, if he were with us, would have favored a diagnosis of sarcoidosis on the radiographic evidence of paratracheal adenopathy which he thought to be pathognomonic. In reference to pathognomonic signs, I always remember the warning of one of my teachers: "diagnoses are not cranes that can stand on one foot".

Dr. John F. Dunkel, E. Lansing, Mich.: I wonder if one could consider the possibility of two separate conditions, that would explain the lung changes and the rib lesions.

Dr. Dahlin: I appreciate Dr. Azar's comments. We tried to say it in a different way; really, we made a diagnosis of sarcoidosis by exclusion. Although I said tuberculosis, I have to bow to the negative cultures which would lead me, with reluctance, to a diagnosis of sarcoidosis. I would not advise further biopsy since the patient is doing well.

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Pygott: Sarcoidosis in Bone. Post-Grad. Med J. **46:** 505-507, 1970.

Kelly, P. J. & Karlson, A. G.: Musculoskeletal Tuberculosis. Mayo Clinic Proceedings. **44:** 73-80, 1969.

2. Chondroblastic Osteosarcoma of a Rib

Contributed by **V. M. Arean, M.D.** and **E. H. Braukman, M.D.**,
St. Petersburg, Fla.

The patient was a 79-year old man in November, 1973, when he presented with a painless tumefaction of the left side of the chest wall, which had been growing for two years. On examination there was a nodular mass 5x7 cm overlying the 8th left rib anteriorly. The serum calcium, phosphorus and alkaline phosphatase values were all within normal limits.

Dr. Hodes: The prime clinical feature is the presence of a painless tumor in the chest wall known to be enlarging for at least two years. Obviously the lesion arises in the rib.

Were this an inflammatory process, an osteomyelitis arising in the rib, one would expect pleural or pulmonary reaction to its presence. There is none. Instead there is a peculiar calcified debris which extends into the chest as well as beyond the chest wall. On close inspection the calcification is flocculent. It looks more like calcified chondroid matrix rather than calcified osteoid matrix.

Cartilaginous tumors are grossly classified as central or eccentric. The central lesions which start in the medulary canal are usually painful. Contrariwise the eccentric malignant cartilaginous tumors commonly grow without producing symptoms.

Of all malignant primary tumors involving the ribs, the myeloma is the most common. Secondarily come the osteosarcomas or chondrosarcomas. The flocculent character of the calcification suggests we are dealing with calcified chondroid matrix because of which we believe we are dealing with, a malignant bone tumor.

Fig. 1—Flocculent calcification around left eighth rib with no neighboring signs of inflammation.

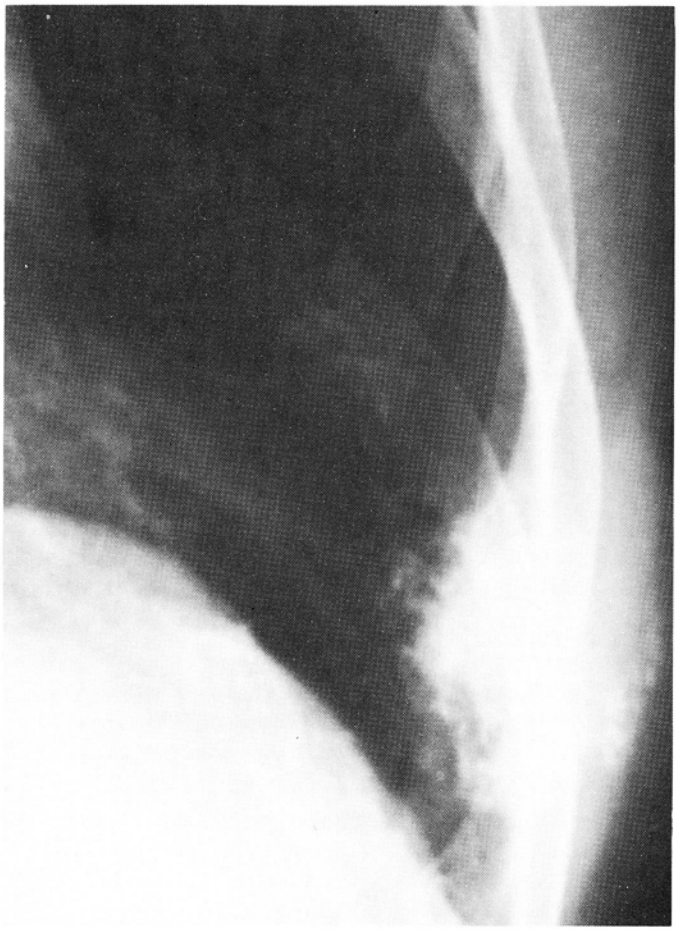
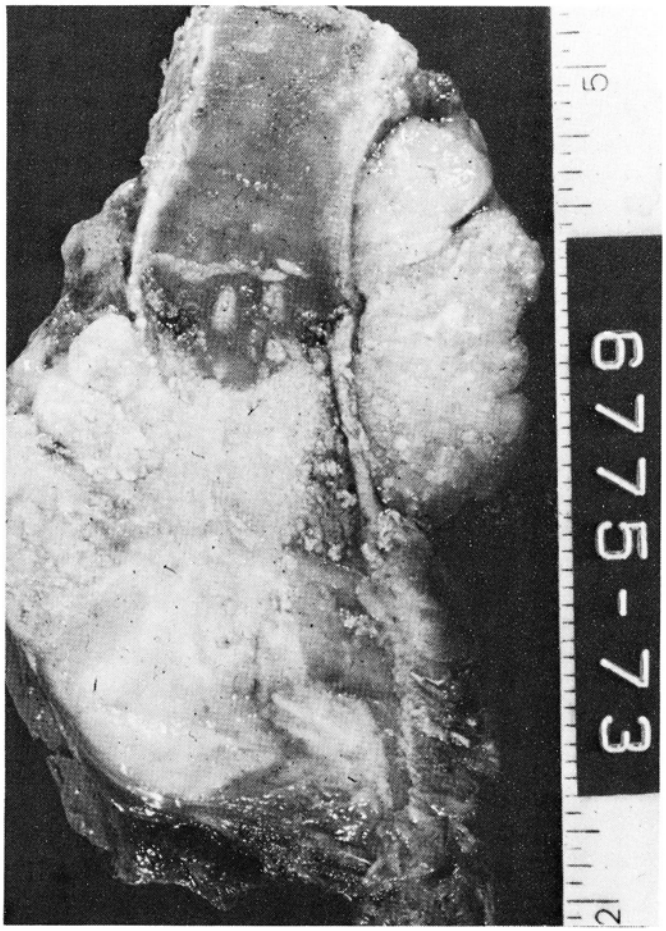


Fig. 2—Surgical specimen of rib with lobulated firm tumor replacing the bone.



Dr. Hodes' impression: Chondrosarcoma

Radiologic Impressions Submitted:

Chondrosarcoma	116
Osteosarcoma	07
Metastatic tumor	07
Fibrosarcoma	04
Plasmocytoma	02
"Lymphoma"	02
Others	04

Dr. Hodes: A painless tumor in the rib, in the left lower thorax, which on close inspection demonstrates no reaction within the lung itself, would exclude an active inflammatory process. We notice that the tumor mass which arises in the rib extends beyond the thoracic cavity as well as inside of the cavity, but the hallmark of this patient's disease is this peculiar flocculent material that we see distributed throughout the soft tissue mass extrinsically, and the soft tissue mass within the thoracic cavity. Now this calcified tumor matrix, this calcification, has the appearance of calcified chondroid, and because of this, one would expect that this is a chondrosarcoma. I leave you with one other thing that oftentimes guides me and that is the question of pain. Usually the centrally placed chondrosarcomas are associated with pain. The ones that start outside of the bone; for instance from an osteochondroma, are more apt to be less painful and the patient is in the age group for chondrosarcoma, and so this is the diagnosis we submitted. I couldn't quibble with osteosarcoma except for the fact that I thought that the ossified matrix was more that of cartilage; also in my own experience, I think chondrosarcomas are much more common than osteosarcomas arising in bone. Metastatic tumor? You would have to explain this peculiar calcification in the soft tissue mass. Fibrosarcoma is always a good diagnosis in the aged; particularly if you are not sure what it is, because it may prove to be that! Plasmocytomas with bone reaction are very unusual. Dr. Dahlin and I did have one such tumor at a seminar in Miami, several years ago, which was an osteoplastic lesion and proved to be a myeloma, but on further investigation, it was a myeloma that had been treated.

Dr. del Regato: The majority of our correspondents submitted an impression of chondrosarcoma. Dr. J. B. Dennis, of Ann Arbor, questioned the possibility of osteosarcoma and Drs. M. Childress and L. Bigonfiari, also from Ann Arbor, suggested metastatic carcinoma.

The University of Missouri radiodiagnostic computer diagnosed chondrosarcoma.

Operative findings: On November 28th, 1973, a resection of the anterior half of the left 9th rib was done. The specimen measured 11 cm in length and was 8 cm in width at its largest point. It contained a lobulated very firm tumor, 7x5 cm, which filled the intercostal space; it was blue-white with pink and ivory color areas, and replaced completely the cancellous and cortical bone.

Dr. Dahlin: This is a malignant tumor and I am comforted by the fact that our radiologist Dr. Jack Beabout feels that the roentgenographic shadows are those strongly suggestive of a malignant tumor. In some portions of it there is a poorly formed somewhat degenerative cartilaginous background suggesting that there may have been an indolent, slowly progressing cartilaginous tumor in this patient. The cartilaginous component which dominates the histologic field is surrounded however by pleomorphic hyperchromatic malignant and even osteoid-producing cells. Accordingly, pre-dominantly we have a chondroblastic osteogenic sarcoma. In other zones, however, the malignant cells are very spindling and taken by themselves would be diagnostic of fibrosarcoma. Within the more anaplastic spindle cell elements there appears to be osteoid produced by the malignant cells as well.

The differential diagnosis in this case revolves around what is the best terminology for the lesion. With the tissue available and as indicated above I think it should be called a chondroblastic osteosarcoma. The degree of dedifferentiation (degree of malignancy) indicates this is a highly anaplastic lesion and should be graded 3 or 4. It is probably academic as to what definite category one wishes to relegate this case. It is even reasonable to wonder whether an unprovable but markedly lower grade cartilaginous tumor has undergone dedifferentiation to produce this anaplastic lesion.

Dr. Dahlin's diagnosis: Chondroblastic Osteosarcoma (Grade IV).

Histopathologic Diagnoses Submitted:

Chondrosarcoma	59
Osteosarcoma	12
Rhabdo—, fibrosarcoma	11
Metastatic tumor	06
Others	21

Dr. Dahlin: Notice, although this is very chondroid, this looks like a tumor that might be more active. You'll notice that the majority has called this chondrosarcoma. As I indicated, I would not quarrel with that characterization, but I think that it is important for us to recognize that the average chondrosarcoma in the chest wall does not look like this tumor, so you should qualify the designation of chondrosarcoma, as far as I am concerned. I think this tumor is definitely producing matrix so that Rhadbo- and Fibrosarcomas are not countable, and I did not see any areas in this that looked like metastatic carcinoma to me.

Dr. del Regato: Dr. F. Cabanne, of Dijon, France also submitted a diagnosis of osteosarcoma, with fibro-and chondromatous contingents. Dr. F. Schajowicz, of Buenos Aires, preferred chondrosarcoma and suggested that someone would call it de-differentiated chondrosarcoma; Dr. A. D. Johnston of New York, and Dr. Suzanne Spanier of Gainesville, Fla. did. Dr. W. K. Bullock, of Los Angeles, preferred malignant

fibro-xanthoma. Dr. H. N. Hadders, of Groningen, Holland, offered chondrosarcoma with progression to fibrosarcoma. Dr. L. Lowbeer of Tulsa, favored metastatic spindle-celled carcinoma.

Dr. Lent C. Johnson, AFIP, Washington, D.C. wrote: This is a calcifying chondroma that has undergone malignant transformation. Most of the section is a mass of spindle cells and some xanthoid cells, neither of which would lead one to suspect cartilaginous origin.

Subsequent History: In November 1974, the patient was reported in good health—in his 80th year. On March 7th, 1975, a follow-up examination done at our request for the purposes of the Cancer Seminar, revealed the presence of a 2 cm nodule in the left pulmonary base near the costophrenic angle and three other smaller nodules in the left upper lobe and behind the heart. Dr. Braukman considered them as metastatic.

Dr. Sim: From a clinical standpoint, we must consider the fact that ⅔ of these lesions of the rib are malignant. Dr. Dahlin reported the Mayo Clinic experience on 145 primary tumors of the rib and sternum in 1957. In this series 68% of these tumors of the ribs were malignant. The commonest malignant lesion of the rib is a chondrosarcoma. Forty of the 145 were chondrosarcoma. We would, of course, investigate the possibility of pulmonary metastasis and other evidence of systemic spread that is frequent in cases such as this. This would include bone scans, whole lung tomograms, etc. From the point of view of treatment, a lesion such as this poses a tremendous therapeutic challenge. Radical en bloc resection is the treatment of choice. In recent years with a better knowledge of pulmonary physiology we have been able to resect large portions of the rib cage and maintain good respiratory function. In this case, location of the lesion in the neighborhood of the diaphragm must be considered and if indeed the diaphragm is involved with tumor, then a portion of the diaphragm must be included in the resection as well. With modern methods one can subsequently reconstruct the chest wall.

Dr. M. Landa, Fargo, No. Dakota: I'd like to ask Dr. Hodes if he has ever seen calcification like this in osteosarcoma?

Dr. Hodes: Whereas anything can happen in medicine, one would not expect this type of calcification in an osteosarcoma. This calcification is fluffy, has a cotton-wool or popcorn-type of

Fig. 3—Malignant tumor formed predominantly by cartilagenous tissue (x 250).

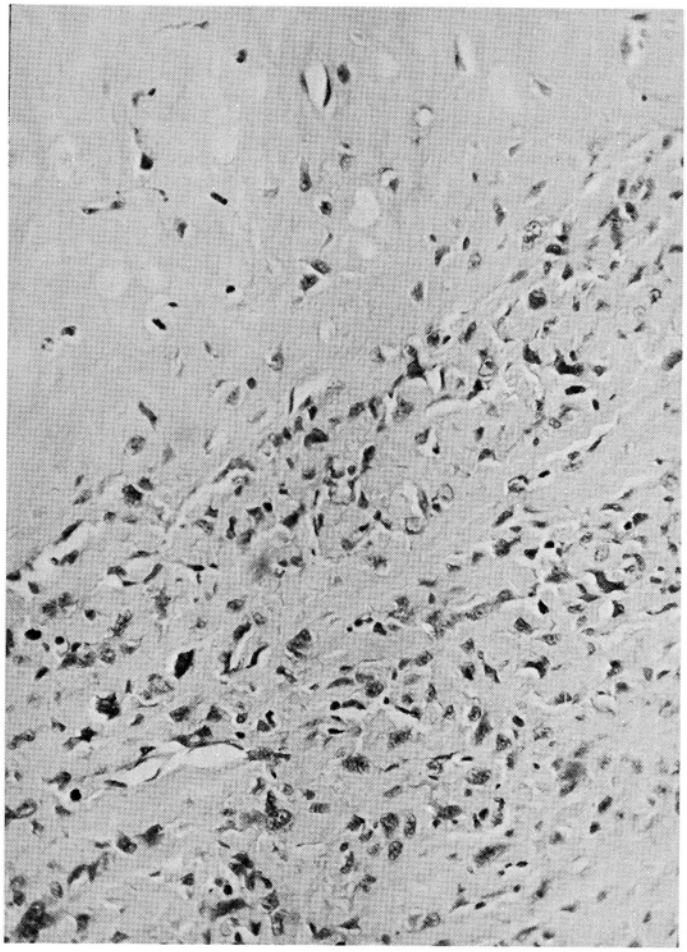
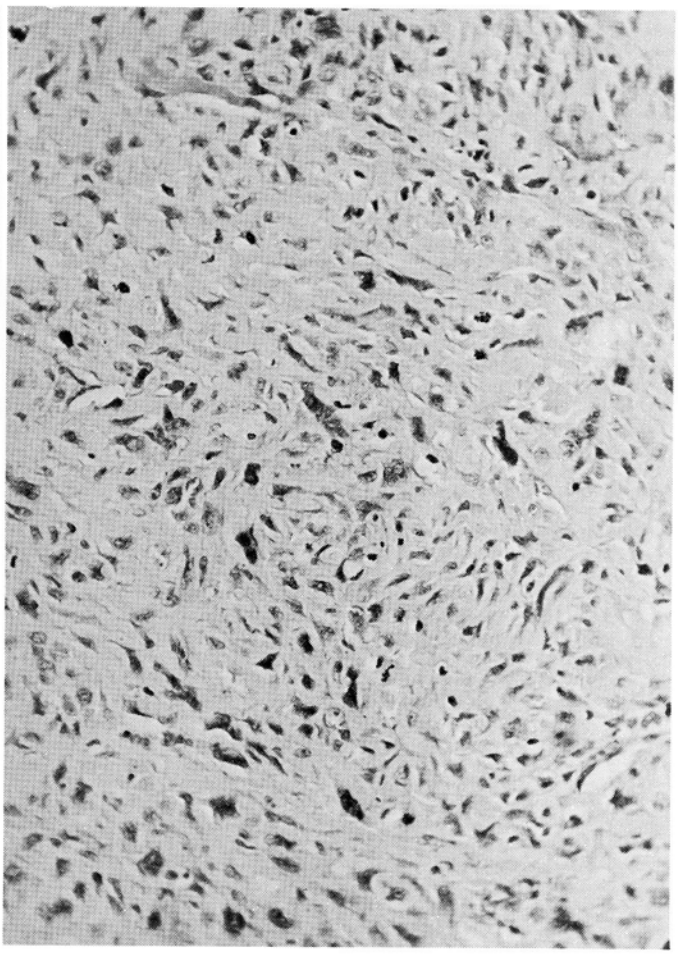


Fig. 4—Pleomorphic appearance with spindle cells (x 250).



configuration, but the inference is calcified chondroid matrix rather than calcified bone matrix. Statistically, chondrosarcomas are found more commonly in ribs than osteosarcomas. Most common of all, of course, are metastatic lesions including myeloma. I have similar concern whenever I see a lesion in the sternum. These, too, usually prove to be malignant although no one will gainsay the possibility of osteomyelitis. Yet one should be able to differentiate the two.

Dr. A. Morales, Miami, Fla.: I wonder when do you draw the line between osteo and chondroblastic.

Dr. Dahlin: I don't think it is always possible to draw a line between these two lesions. What he asked is the difference between a chondroblastic osteosarcoma and an undifferentiated chondrosarcoma. Sometimes, it is obvious that the bone is not malignant, but sometimes it is impossible for me to be sure; usually, if it is a high-grade lesion, a more active lesion, in areas of spindle cells, I think there's a strong capability for metastasizing and I sort of use that as pushing towards osteosarcoma. I think the final interpretation of this case, of dedifferentiation into a more active lesion is a likely ballot. Different areas with this sternum might allow one to make quite different interpretations of the capability of the lesion. I think whenever you have it as active—as this was in part of the tissue I received—with anaplasia, that the likelihood of the metastases is high, in the range of 80%. That is why I thought that this was over the fence—well over the fence—for osteosarcoma.

Dr. Charyulu, Miami, Fla.: I have one comment on the classification of bone tumors you showed in a slide, based on the therapeutic modality, namely radio-resistant or radiosensitive tumors. Experience of most radiotherapists is consistent with our observation that some of the so-called radio-resistant tumors, such as chondrosarcomas or osteosarcomas; can be sometimes radiosensitive. The radiosensitivity or resistance depends upon the cell biological factors characteristic of a given tumor, at any given point of time in its natural history. Thus, an osteosarcoma could be radioinsensitive when the tumor is highly differentiated and has a low growth fraction; whereas the same tumor in the same patient may exhibit radiosensitivity later in its evolution, when the cells become less differentiated and the tumor has a higher growth fraction. Moreover, the radiosensitivity or otherwise, as commonly judged by gross disappearance of mass, depends upon the bulk of tumor cells, a higher initial cell number making the tumor less radiosensitive. In the light of these concepts, I believe that the classification of tumors based on radiosensitivity or otherwise, is out of place at this time.

Dr. del Regato: I think what is involved in this is a question of semantics, a consideration of the meaning of the word, **radio-sensitivity.** Originally, radio-sensitivity was attached to the promptness of the response and in that effect, such tumors as Hodgkins lymphosarcomas are the most radio-sensitive and such tumors as adeno-carcinomas are the least radio-sensitive. The word radio-resistant was given instead of least radio-sensitive and that's where the confusion comes in. In some of these tumors, provided they receive a sufficient amount of radiations, an adequate amount of radiations under the circumstances, the tumor would eventually regress even though it might take—as in the case of adenocarcinomas of the prostate—weeks and months for them to disappear completely, but they do disappear, if they are adequately irradiated. It is only a matter of difference in the rapidity of response. I have irradiated and controlled a large chondrosarcoma of the pelvis that was beyond a hemipelvectomy. Nevertheless, we do not advocate radiotherapy as an alternative to surgery in most instances.

Dr. R. Cavanagh, Boynton Beach, Fla.: Dr. Dahlin showed some very fine radiographic examples of chondrosarcomas, but in his comments on the radiographic findings, I think that he may have given the impression that in many of those cases the presence of calcification, or the pattern of calcification, indicated that the lesion was a chondrosarcoma. Now, I'm not sure if he meant to do that. If he did, I would disagree that the presence of calcification or the pattern of the calcification indicates that a tumor is a sarcoma, although it may indicate that the nature of the tumor is cartilaginous.

Dr. Dahlin: I'm a pathologist and I agree. It just tells us that it's cartilaginous, not whether it's benign or malignant. Is that right Dr. Hodes?

Dr. Hodes: Yes.

Dr. E. Murphy, Mexico City: I understood—this question was to you Dr. Sim—that later on the man developed a solitary metastases in the other lung. Is that so? (Answered: That was not so.) Well then, supposing, in another case in the same situation, if a metastases had been solitary—at least apparently solitary—would there be any point in resecting it?

Dr. Sim: I think this is an excellent question and illustrates very well the aggressive philosophy we have had in the management of these patients in the past few years. The previous approach to such a problem was to observe a solitary metastatic lesion in the lung for two or three months and if there is no further evidence of metastatic lesions, then the patient would be considered a candidate for resection of the pulmonary lesion. Our present protocol for the postoperative management of patients with osteo-

genic sarcoma calls for a stereo PA and lateral chest films every month and lung tomograms at three month intervals. If a pulmonary metastatic lesion develops we recommend thoracotomy and resection of the lesion. This aggressive surgical philosophy has been expanded to other sarcomas including soft tissue sarcomas. With improvements in chest surgery and improvements in knowledge of pulmonary physiology, subpleural resection of these lesions gives very little morbidity to the patient. With the recent advances in adjunctive chemotherapy and immunotherapy in improving the prognosis in patients with sarcomas with minimal residual disease, such an aggressive surgical approach to the management of patients with multiple surgically resectable pulmonary metastatic lesions has been very gratifying in our experience.

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3. Fibrous Dysplasia of a Rib

Contributed by **M. R. Abell, M.D.** and **Wm. Martel, M.D.**, Ann Arbor, Michigan

The patient was a 53-year-old woman in March, 1974 when she complained of pain in the right shoulder and loss of strength in the right hand. A tumor had been removed from the right side of the neck two years previously and a sub-total thyroidectomy had been done 16 years before that. On examination there was a deep-seated mass beneath the muscles of the neck and the right scapula under the scar of previous excision. The alkaline phosphatase was elevated: 147 I.U.

Dr. Hodes: The pertinent clinical data include the clinical story that a tumor had been removed from the right side of the neck two years previously and sixteen years before that the patient had had a sub-total thyroidectomy. A deep seated mass could be felt beneath the muscles of the neck and the right scapula under the scar of the previous surgical procedure. At the present time the patient had lost strength in the right hand

Fig. 1—Large intrathoracic mass, apparently extrapleural.

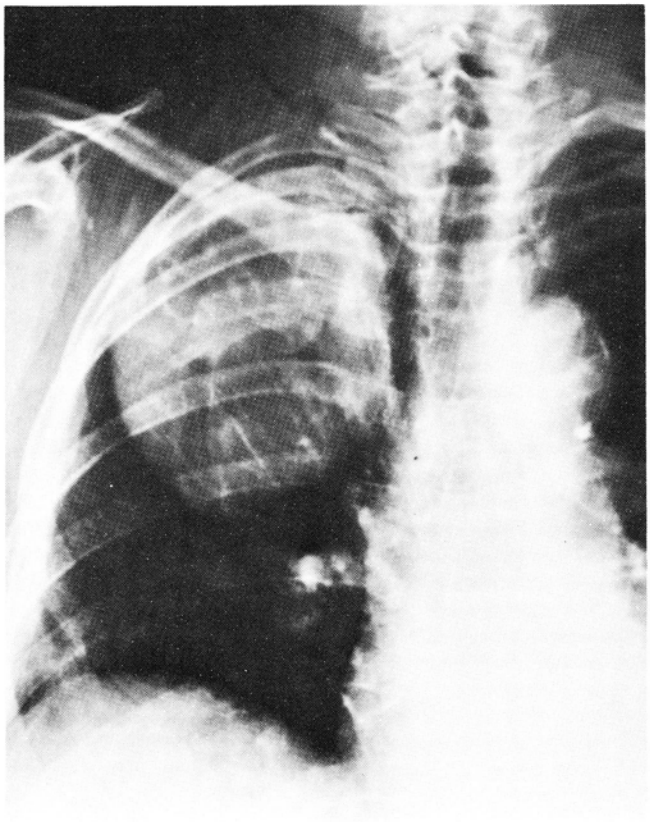
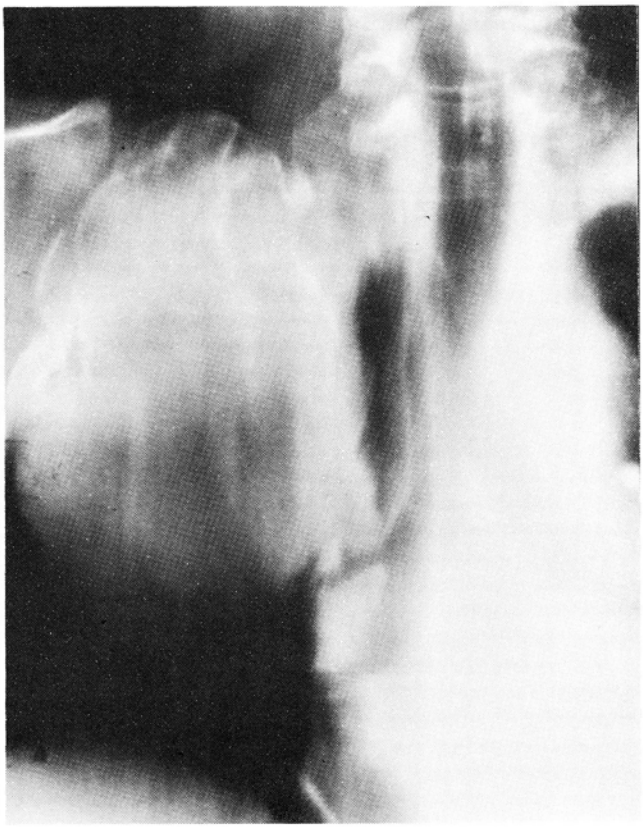


Fig. 2—Tomogram showing a lobulated appearance.



probably due to involvement of the brachioplexus.

Our concern is not the large mass which apparently is extrapleural but obviously extending within the thoracic cavity. Central to the diagnosis is the obvious appearance of an expansile lesion involving the first rib which starts at its costovertebral articulation. The body section films reveal its lobular configuration which along the superior margin seems encapsulated by a very thin rim of cortex. One sees no bone elsewhere either within the tumor mass or around its remaining circumference. The supraclavicular extension of the mass is obvious; apparently the clavicle itself is unaffected because the mass lies posteriorly and does extend into the middle mediastinum as manifested by the marked distortion of the upper lobe bronchus on the right side.

Because we are reasonably certain this is not a pulmonary lesion but a lesion arising in the first rib, among the abnormalities to be considered are metastatic disease, primary pleural lesion secondarily involving the rib, primary cartilaginous tumor, myeloma, aneurysmal bone cyst and even fibrocystic disease.

I am excluding a cartilaginous tumor because I can see no evidence of calcified chonroid matrix. I am also excluding metastatic disease because the shell of bone that envelopes the tumor particularly is so clearly defined. Myelomas destroy bone; this lesion is expanding it. We are left, therefore, with an aneurysmal bone cyst or fibrous dysplasia.

Apparently this is a monostotic lesion which has recurred. I would expect that fibrocystic disease properly treated (this patient was operated upon previously for this process) would not continue to develop. Furthermore, this has a "blown out" appearance so characteristic of aneurysmal bone cysts. The patient's age, fifty-three, is somewhat beyond the usual age for aneurysmal bone cysts which tend to occur earlier in life. And while it is not important, there is no history of trauma.

Pleural reaction is obvious in the right hemithorax which may have been the result of previous surgery, or it might conceivably be a slow leak of blood into the extrapleural space from a bloody lesion. Also, it might be the result of whatever surgical procedure it was that removed a portion of the 5th rib on the right side, reference to which was never made. We are told nothing about the nature of this rib lesion which was previously operated upon. Perhaps it, too, was cystic in nature. If it was then we have a polyostotic process which would militate against an aneurysmal bone cyst. Because we are told nothing about this resected rib, I am presuming it had nothing to do with the case. Thus, I believe we are dealing with a huge aneurysmal bone syst. However, if a previous film of this chest revealed a similar cystic lesion in the resected rib, the diagnosis obviously would be polyostotic fibrous dysplasia.

Dr. Hodes' Impression: Aneurysmal Cyst.

Radiologic Impressions Submitted:

Metastatic tumor	36
Plasmocytoma	28
Fibrosarcoma	20
Neurofibroma	09
Chondrosarcoma	09
Aneurysmal cyst	09
Fibrous Dysplasia	07
Others	23

Dr. Hodes: I can't disagree with a diagnosis of metastatic tumor. There are lesions that do cause this bulbous type of bone expansion and I considered that. I did not think it was a plasmocytoma. Fibrosarcoma is capable of doing anything. I don't believe that a neurofibroma would have done that to the proximal portion of the bone, but maybe. Chondrosarcoma, I considered but excluded because it did not have any of the calcified chondroid matrix and I'm glad to see that a few considered aneurysmal cyst and fibrous dysplasia.

Dr. del Regato: Dr. M. Corte-Real, of Lisbon, suggested a Schwannoma. Dr. M. Levine, of Vancouver, Washington, offered neurilemoma. Drs. J. Ambrosini, of Ann Arbor and L. N. Schulz, of Cincinnati, preferred neurofibrosarcoma. Dr. M. Valette, of Creteil, France, offered ossifying fibromatosis.

The University of Missouri radiodiagnostic computer diagnosed chondrosarcoma.

Operative findings: On April 10th, 1974 the first and second right side ribs were resected together with a portion of the clavicle. The nerves and vessels were not interfered with. The specimen contained a mass 10x8x7 cm, apparently well encapsulated, which spread between the ribs. On cross section, the mass was light gray to yellow in color with scattered cystic areas surrounded by hemorrhage and necrosis.

Dr. Dahlin: One is tempted to think in terms of this being a malignant tumor because of the large shadow produced in the chest roentgenogram. Careful study fails to reveal any evidence of malignant tumor. The proliferating cells are nearly all fibroblastic and show considerable collagen production. Here and there old iron pigment manifested by brown staining phagocytes are present. The degree of cellularity varies somewhat from area to area. Essential to the diagnosis is the component of meaningless masses of osteoid in trabecular arrangement that are present. Some of these are "T" and "Y" shaped. They do not tend to anastomose one with the other.

In the differential diagnosis one must consider a bone forming sarcoma but no anaplasia is present and the gradual transitions of the essentially fibroblastic cells into those capable of producing osteoid trabeculae appear diagnostic.

When malignant change supervenes in fibrous dysplasia it is nearly always very highly anaplastic and transitional forms practically do not exist.

Dr. Dahlin's Diagnosis: Fibrous Dysplasia

Histopathologic Diagnoses Submitted:	
Fibrous dysplasia	33
Fibrous histiocytoma	12
Ossifying fibroma	11
Fibrosarcoma	13
Osteosarcoma	06
Others	29

Dr. Dahlin: The majority recognized fibrous dysplasia. Fibrous histiocytoma was thought of because of the whirling pattern of the fibroblastic tissue. I don't think that's correct because it should not have an anaplastic osteoid. Ossifying fibroma is not the reasonable diagnosis for bone lesions. Lent Johnson and a few others know how to diagnose this thing, but most people don't; I think it's essentially impossible. The term, ossifying fibroma, as used in the literature is meant to imply that one sees a lesion with greater aggressiveness than fibrous dysplasia should have. I don't think that there's really good evidence that it is a fact. I don't think this tumor is malignant and, therefore, fibrosarcoma and osteosarcoma are not in.

Dr. del Regato: Dr. H. A. Sissons, of London, also submitted a diagnosis of fibrous dysplasia. Dr. Y. LeGal, of Strasbourg, suggested dermatofibrosarcoma. Dr. L. V. Ackerman, of Stony Brook, found invasive fibromatosis and suggested the possibility of low-grade fibrosarcoma. Dr. Weil-Busson, of Strasbourg, also suggested fibrosarcoma. Both Ackerman and Weil-Busson questioned if the patient had received radiotherapy. Dr. H. Spjut, of Houston, suggested the possibility of a fibrous histiocytoma.

Dr. Andre Warter, of Strasbourg, categorically offered a diagnosis of malignant pleomorphic fibrous histiocytoma. Drs. S. A. Jacobson, of Vancouver, Washington, and M. R. Abell, of Ann Arbor, called it an ossifying fibroma. Dr. E. Lichtenberger of Bogota, interpreted it as an old healing hyperthyroid lesion.

Dr. Lent C. Johnson, AFIP, Washington, D.C. wrote: This is what I call a central fibroma. Central fibromas are very treacherous; they do not look particularly malignant, yet they continue to grow, expand, infiltrate, and even metastasize.

Subsequent History: In June 1974, the patient was found in good health.

Dr. Sim: From a clinical standpoint such a large and extensive lesion in this area is worrisome. Clinically this large polylobulated mass with lytic changes in the first rib is already manifesting symptoms of a thoracic outlet syndrome. Certainly in the initial workup we must consider a venogram or arteriogram which will

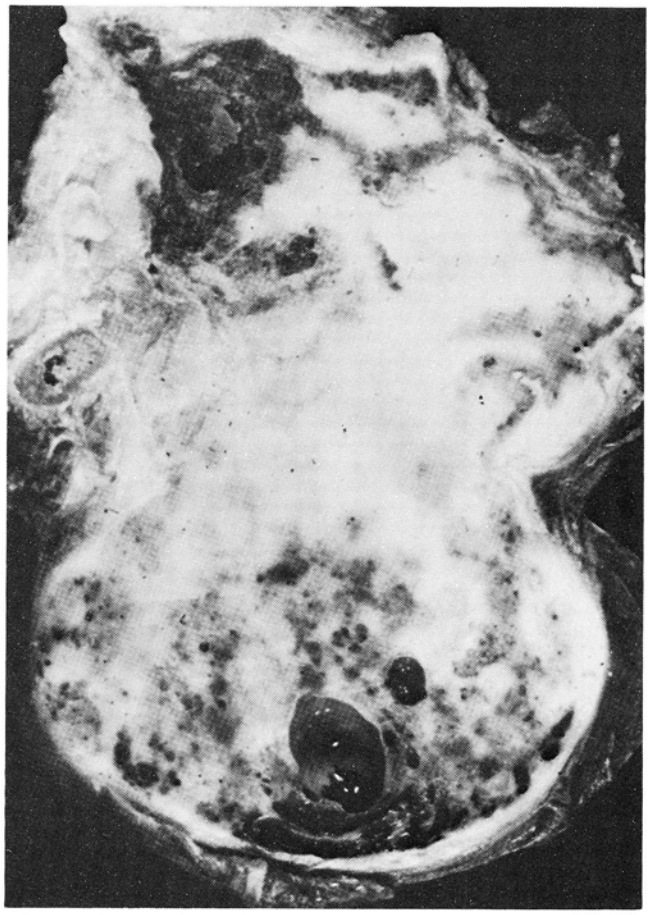


Fig. 3—Surgical specimen of large tumor spreading between ribs.

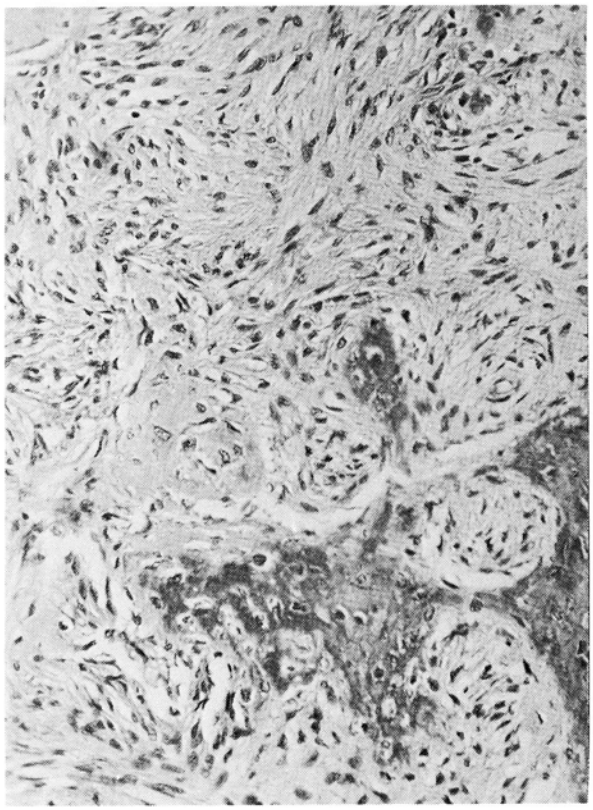
be helpful in planning the surgery. One does not want to make the patient any worse than his preoperative status and it would be advisable to document any previous neurological changes. An EMG would be helpful in this regard. This extensive lesion must be excised and we would proceed with an excisional biopsy through a carefully planned surgical approach. This might best be approached through a posterior (Paulsen) approach. A rather extensive removal of the entire upper rib cage could be performed if this were necessary for malignant tumor. In this type of monostotic fibrous dysplasia, a complete excision should be curative to the patient. In our series of 145 tumors of the ribs and sternum, fibrous dysplasia was the most common benign tumor to the ribs. In Harris' description of the natural history of fibrous dysplasia, 5 of his 13 patients with monostotic disease had rib involvement; excision cured all of these cases.

Dr. A. Morales, Miami, Fla.: This was one of the cases, Dr. Dahlin, where you did not agree with Dr. Hodes' interpretation, and with the diagnoses made in our department, of ossifying fibroma. We based our interpretation, primarily, on the films and on the fact that this tumor is more aggressive than fibrous dysplasia. In addition, there is lamellar bone around the central

area of bone formation. I wonder if you would elaborate more about your ideas on ossifying fibroma?

Dr. Dahlin: The literature on ossifying fibroma, that I am familiar with, is almost all related to the jaws. I think the best articles on the subject, at least I can understand them better, are written by Walgren & Gian-Santi from Emory. These people divided the fibro-osseous neoplasms of the jaws into fibrous dysplasia and into fibro-osseous lesions. They avoided this nomenclature confusion, if you will. I think if you take the fibro-osseous lesions in the jaw; first of all, they are all benign so it really doesn't make much difference what you call them,—I think that fibrous osteoma or ossifying fibroma is not a clinical diagnosis, outside the jaws. The lesions that we call that—I don't know what Lent Johnson meant by central fibroma of the bone; we don't seem to get those in Rochester. Maybe we're lopping too much when we call a lesion like this fibrous dysplasia but I think that the irregular masses of bone and so forth, fit what we call fibrous dysplasia. The special studies like those with polarized light, ossifying fibers and so forth, have made nice articles but I don't think they help us solve the problem as to what the name of these things should be. I think we have other categories that we can put bone lesions into, if they are outside the jaw. We don't have to conjure up the term of ossifying fibroma. I really don't know how to diagnose that; I notice that Dr. Jacobson suggested that as a possibility. Maybe he has some reasons?

Fig. 4—Fibroblastic cells with meaningless masses of osteoid, varied degrees of cellularity and considerable collagen production (x 250).



Dr. S. Jacobson, Vancouver, Washington: In general, I think what I call ossifying fibroma looks different from what I call fibrous dysplasia. Fibrous dysplasia has typically almost mathematical spacing of the fibroblasts and of the bone trabeculae. When I saw the bone growing irregularly without any particular spacing, I call it ossifying fibroma, especially if the fibroblasts too are irregular in their distribution. As a few of you perhaps know, I've made a study of animal bone tumors. Something that looks like fibrous dysplasia, as we understand it in man, certainly the polyostotic type, is rare in animals. On the other hand, a fibro-osseous lesion is common in animals. In fact, in the horse, it is the commonest of all bone tumors. I have not seen anything like fibrous dysplasia in the horse. I believe, therefore, that these are two separate and distinct lesions.

Dr. Donald Eisert, Milwaukee, Wisconsin: Dr. Dahlin referred to radiation-induced sarcomas. This is an area of great confusion with many zones of gray. It is virtually impossible to make the distinction between radiation-induced sarcoma and spontaneous dedifferentiation to sarcoma unless you know the natural biological behavior of a tumor. For example, earlier discussion of chondrosarcoma pointed out that these were tumors that dedifferentiated spontaneously. This is known to occur without the patient's having had radiation therapy. The other thing is that if you wrote on the potential of radiations to induce sarcoma and noted only whether the patient had been irradiated or not, you might misleadingly conclude the patient had radiation-induced sarcoma. You better make sure that the area where the sarcoma occurs is actually in the field of radiation. I am not denying that radiation therapy induces sarcoma, but we have to distinguish between the sarcoma induced by radiation and a sarcoma arising in an irradiated patient. It is not uncommon in other areas to have otherwise unexplained findings attributed to radiation therapy even though radiations were not directed at the area in question. I think the distinction is important and unless carefully analyzed the data on the potential of radiations to induced sarcomas should be interpreted with caution.

Dr. del Regato: Another one thing I will allow myself to add is: just because you find toads after the rain, it has not necessarily rained toads!

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4. Giant-Cell Tumor of the Distal Femur

Contributed by **Luther W. Brady, M.D.**, Philadelphia, Pennsylvania

The patient was a 36-year-old woman in November, 1968 when she related that she had fallen on her right knee one year previously; an, at first, intermittent pain on the medial aspect of the knee had persisted for the last five months. She also gave a history of thyroidectomy six months before examination. The right knee joint was enlarged and there was evidence of atrophy of the gastrocnemius and quadriceps muscles. The serum sodium, potassium, chloride and alkaline phosphatase were all within normal limits; the blood count was normal.

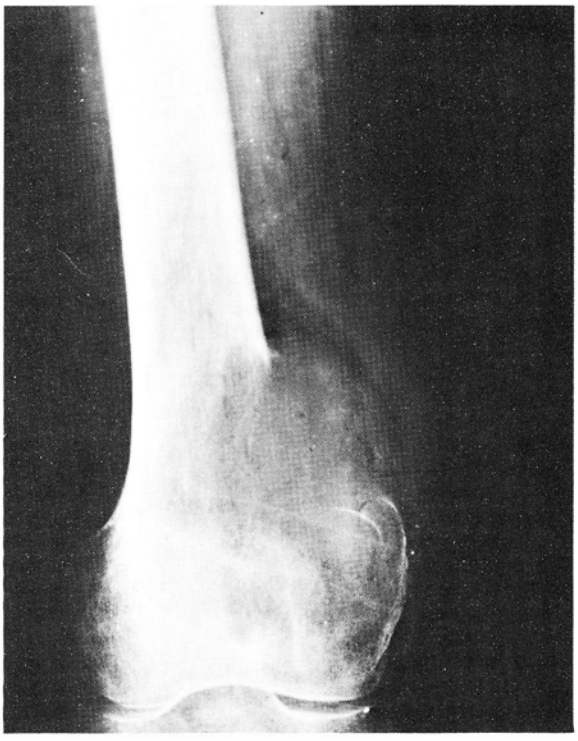
Dr. Hodes: Clinically significant is the history of trauma one year previously followed by localized swelling and muscle atrophy. The thyroidectomy six months before this examination may bear upon the ultimate diagnosis. The patient is thirty-six.

What a beautiful demonstration of a soft tissue mass outlined by a fascial plane. We have only the one sagittal projection; we know nothing about the lateral view; I imagine it added nothing of importance.

Noteworthy is the fact that there is practically no soft tissue reaction beyond the confines of the soft tissue tumor.

Careful inspection of the destroyed bone reveals no sharp transition between the mass itself and the perifocal bone. The lesion extends to the juxta-articular portion of the femur in asymmetrical manner and is expanding the medial condyle of the femur that it is eroding.

Fig. 1—Lytic lesion expanding the medial condyle and extending to the juxta-articular position of the femur.



Classical giant cell tumors occur in the age group between twenty and forty (mean of thirty-two) and described as eccentric asymmetrical periarticular abnormalities. These criteria are amply demonstrated by this bone lesion. The question of trauma one year previously makes one wonder as to the possibility that this might be an aneurysmal bone cyst rather than a giant cell tumor. And that possibility will continue to exist. I am impressed by the appearance of the cortex just proximal to the main soft tissue mass which cortex seems to be deflected beyond the normal cortical line. Occasionally one sees malignant giant cell tumors of tendons secondarily involve bone. But this soft tissue mass seems too well encapsulated to be the ordinary synovial or tendon malignancy.

Because this is a periarticular asymmetrical bone lesion which appears to arise within the medullary canal and extend beyond it destroying the cortex in one area and displacing and thinning it in another, I feel we are dealing with a giant cell tumor. I am not prepared to say whether this is benign or malignant.

Dr. Hodes' Impression: Giant-Cell Tumor

Radiologic Impressions Submitted:

Metastatic tumor	45
Giant-cell tumor	31
Fibrosarcoma	30
Osteosarcoma	19
Synovial sarcoma	10
Reticulum-cell sarcoma	07
Chondrosarcoma	04
Others	07

Dr. Hodes: I think of metastatic lesions when I get into the older age group, beyond the age of 36. The hallmark of fibrosarcoma is a lesion that looks like something but not quite like it. When I've repeatedly looked at it, with misgivings, with mixed emotions, then I back into a diagnosis of fibrosarcoma. I don't believe that fascial plane would have come out so beautifully outlined in a case of osteosarcoma. I would have expected much more irregular lesions, more permeation of the bone itself. I don't believe that a synovial sarcoma would be just this clearly demarcated. I didn't think of reticulum-cell sarcoma because I zeroed in on aneurysmal bone cyst and giant-cell tumor. I saw nothing at all to suggest chondrosarcoma; there is an osteolytic type of chondrosarcoma, but it's unusual. A paraartic-

ular, eccentric, osteolytic lesion of the long bone around the knee at age 36 spells a benign bone cyst or a giant-cell tumor. I say giant-cell tumor, benign, with tongue in cheek.

Dr. del Regato: Drs. M. Viamonte, Jr. of Miami, L. Bigongiari, of Ann Arbor, Jeremy Altman of the AFIP, and M. Valette, of Paris, offered a diagnostic impression of giant-cell tumor. Dr. W. Martel, of Ann Arbor, suggested an aneurysmal cyst. The history of thyroidectomy influenced a great proportion of other radiologists. Drs. G. Lodwick and C. Farrell, of Columbia, Missouri, favored giant-cell tumor.

The University of Missouri radiodiagnostic computer diagnosed fibrosarcoma.

Operative findings: On November 21st, 1968, the lower end of the femur was resected and replaced by a bone graft from the tibia; an arthrodesis of the knee was instituted. The surgical specimen consisted of the distal 11.5 cm of the femur; it contained a tumor which grossly appeared to involve the posterior cortex. On cross section the tumor consisted of gray-yellow transparent material.

Dr. Dahlin: With the bias provided that this is a tumor of the distal end of the femur in a woman of 36 years of age, giant cell tumor becomes a strong probability. Microscopically in this case there are large areas of necrotic tissue which are unrecognizable, but in areas do suggest giant cell tumor because of the ghost-like residue present. In the viable zones the essential feature is a proliferation of mononuclear cells which lack significant anaplasia even though mitotic figures are not difficult to find. Liberally sprinkled amongst the mononuclear elements are benign giant cells. The nuclei of these cells are essentially like those of the mononuclear cells. Here and there a few foam cells have developed in the stroma. There is some early osteoid bone present in the section but the cells within and adjacent to the trabeculae of this bone are not malignant in appearance.

A differential diagnosis is not reasonable in this case because all of the features are those of giant cell tumor. The question that arises is whether one should attempt to grade this tumor with an attempt to predict whether the lesion is apt to recur as they do in about 50% of cases or to become subsequently malignant which development one can expect in perhaps 10% of cases. We have developed no criteria by which such grading is of value. We would not expect this tumor to metastasize except as it does in perhaps 1% of cases in which distant metastases, usually pulmonary, of benign giant cell tumor develop.

Dr. Dahlin's Diagnosis: Giant-Cell Tumor

Histopathologic Diagnoses Submitted:	
Giant-cell tumor	60
Metastatic tumor	21
Osteosarcoma	12
Others	12

Dr. Dahlin: I do not think that the stroma in this lesion was malignant. The tumor may show osteoid, especially after fracture: it's a reactive type of bone that's produced. The presence of bone should not make anyone think that it's malignant. The cells producing the bone have to be malignant for that notion to be proven. I don't know why one should consider metastatic carcinoma on the basis of the histology of the case and the patient's age.

Dr. del Regato: Dr. H. Spjut, of Houston, also made a diagnosis of giant-cell tumor and he noted that there being an epiphyseal extension, there could be an aneurysmal component to this lesion. Dr. L. Lowbeer, of Tulsa, suspected a chondroblastic or fibroblastic osteosarcoma. Dr. W. K. Bullock, of Los Angeles, considered the possibility of a metastatic spindle-cell or giant-cell carcinoma. Dr. Y. LeGal, of Strasbourg had the same, but stronger, inclination. Dr. Juan Rosai, of Minneapolis, preferred a diagnosis of osteosarcoma simulating giant-cell tumor. Dr. Benjamin Castleman, of Boston, felt that the location in the metaphysis, the aggressive involvement of soft tissue and the stromal cells suggest an epithelial origin.

Biopsy of this case was originally examined by Drs. A. Nedwich and J. M. Dolphin, in 1968; they concluded to a malignant giant-cell tumor. Dr. E. E. Aegerter, consultant pathologist, noted the radiographic evidence of destructiveness and reached the same conclusion. He advised against radiotherapy and stated, "a number of such lesions in my collection treated with x-rays have developed into highly malignant sarcomas."

The slides and roentgenograms of this case were also examined, in 1968, by Dr. Lent Johnson, of the Armed Forces Institute of Pathology (Accession Number 1299459) who stated: **"The staff would be hesitant to call the lesion malignant.** The areas of xanthoma cells suggest some moderate involutional changes; the areas of small mononuclear cells suggest excessive degree of activity . . . The size of the tumor is such that if the entire lesion is not removed completely, recurrences are likely to lead to very serious problems in the future. If additional material becomes available, the staff would very much appreciate seeing it. Other areas than those represented in these slides may necessitate a modification of the diagnosis."

In this 1975 Cancer Seminar, Dr. Lent Johnson submitted the following: The significant feature of this giant-cell tumor is too much variation in size, shape and staining intensity of the mononuclear cells and of the giant cells. Therefore, it is malignant. However, this presupposes that the patient is not or has not been recently pregnant.

Subsequent history: The patient has accepted and learned to live with her artificial ankylosis. On September 21st, 1973, five years after her operation, she did not have any evidence of recurrence or metastases.

Dr. Sim: This case points out some of the problems and pitfalls in the management of bone tumors. A delay in diagnosis because of the history of a fall led to disregard of the early symptoms and allowed the tumor to show its aggressive nature, destroying almost the entire distal femur, breaking through the cortex and invading the surrounding soft tissue. I have a great deal of respect for giant cell tumors, particularly when they extend to compromise the integrity of the joint. The other area of challenge is when the soft tissues are penetrated by the tumor.

The recurrence rate is 30% within the first year or two, following curettage, and 50% within five years. I think these tumors do deserve the respect in which we hold them. From the therapeutic standpoint, the extensiveness of the lesion is something we should always consider in recommending treatment. The aggressiveness of the therapeutic approach will depend on whether the lesion is intra-osseous or whether there is frank soft tissue extension of the tumor and the amount of cortical destruction. Generally, in a confined intra-osseous lesion, our approach would be radical curettage of the lesion with complete exteriorization of the lesion completely removing the entire cortex down to the articular surface and perhaps removing two-thirds of the circumference of the bone so that curettage can be done under direct vision. Rather than referring to such a procedure as curettage, I think what we really must stress is that the tumor is excised with a curette. In a lesion as extensive as this, the best chance for the patient is to remove the entire distal femur, since the surrounding shell of bone and periosteum should also be excised. There are several methods of reconstruction. In younger people, we would tend to bridge the defect with a bone graft and knee arthrodesis. D'Aubigne has popularized the technique where a section of the proximal tibia can be divided and slid upward to bridge the defect. In tall individuals, we have taken an appropriate segment of bone from the subtrochanteric area of the opposite leg in order to bridge the defect. This would make the patient shorter but both legs are equal in length and the segmental reconstruction carried out with a knee arthrodesis. We have taken cases such as this and restored the integrity of the distal femur by an implant utilizing a total joint replacement to restore the joint function. These have been holding up very well, but in younger persons, we would resect this lesion and bridge the defect with tibial bone graft.

Dr. Charyulu, Miami, Fla.: In London, years ago, we irradiated many of these patients with about 2,000 rads and the patients went home. Sometimes there was a recurrence or pain, 2 or 3 years later, and they would be irradiated again. There are different types of these tumors with different growth characteristics. A number of patients that were irradiated did well and had no further trouble.

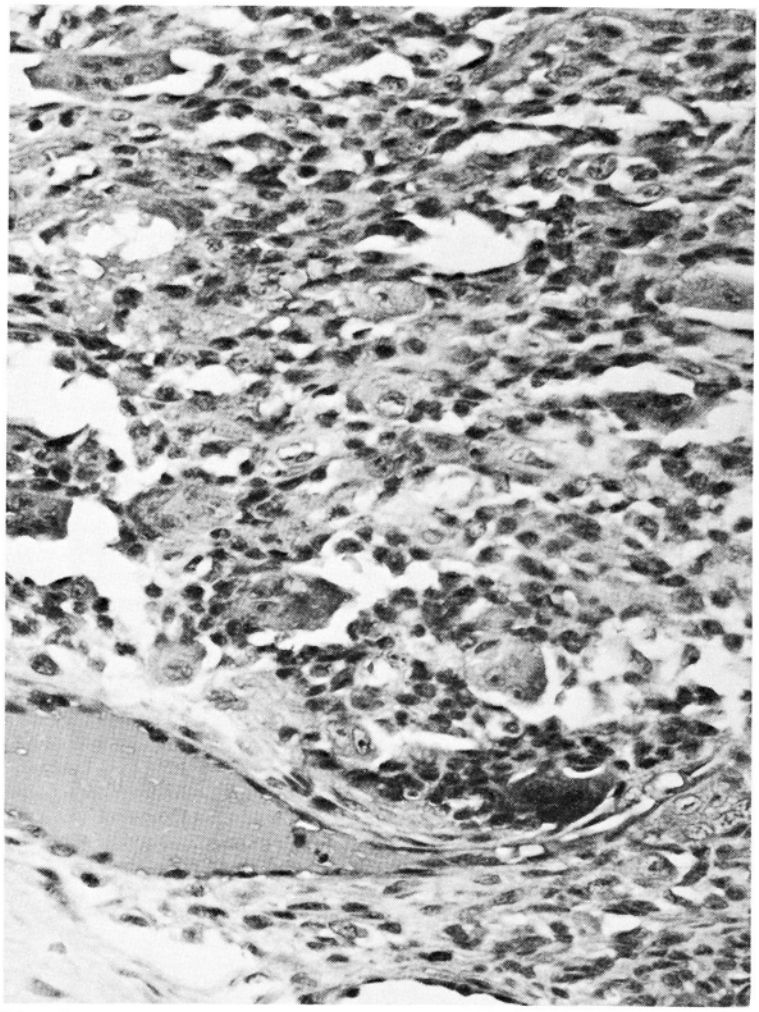


Fig. 2—Areas of ghost-like residue suggesting giant-cell tumor.

Dr. Morales, Miami, Fla.: I was wondering if Dr. Dahlin would comment on the histogenesis of the tumors. I wonder if you believe that there may be a relationship between giant-cell tumor of bone and fibrocystic lesions?

Dr. Dahlin: I don't know the answer to that question. There's going to be a lot written about malignant fibrohistiocytoma of bone in the next few years; maybe we'll learn more about it. At the present time, it seems that the cells that are proliferating in giant-cell tumor are some primitive—some committed mensenchymal cells. Now we know from the bone we see in them, or in metastases from benign giant-cell tumors during soft tissue recurrences, that the cell is capable of producing osteoid, but most of what we see is uncommitted. I don't know if there is a relationship with that and fibro-histiocytoma. I don't know what to believe.

Dr. Padron, Miami, Fla.: I wonder if Dr. Dahlin would explain what is the criteria in making the diagnosis of benign or malignant giant-cell tumor.

Dr. del Regato: Also, Dr. Dahlin, one of the members of the audience wishes to know if you had changed your mind about grading giant-cell tumors.

Dr. Dahlin: I tried to imply that we can't, at least I can't grade giant-cell tumors. To predict whether they are going to have an increased risk of recurrence or whether the tumor actually is in the rare 1% that does metastasize. The lesion that we have called malignant giant-cell tumor is quite different from ordinary giant-cell tumors. It is not a shading into malignancy. When malignancy supervenes, it's usually Grade 4. Once in a while, it's an osteoid-producing sarcoma. When you worry about a slight degree of malignancy in giant-cell tumor, it's probably best just to say, this is a giant-cell tumor.

Dr. Brady, Philadelphia, Penn.: At the request of Dr. del Regato, I talked to this patient yesterday. She was not pregnant. She is now walking without crutches and without a brace, but the fact is that just about 6 months prior to the diagnosis of this tumor, she had hyperthyroidism for which she was operated; she had subsequently been treated with radioactive iodine for recrudescence of the hyperthyroidism. Do you think, Dr. Dahlin, that hyperthyroidism would have had any influence on the appearance and behavior of this particular tumor? Dr. Lent Johnson had inquired originally, as to whether the patient was hyperthyroid or hyperparathyroid; of course, she was not hyperparathyroid.

Dr. Dahlin: I don't know that hyperthyroidism would be related to giant-cell tumor. She must have had two diseases, unless there is a relationship that escapes me.

Dr. Brady: In those individuals with giant-cell tumors who were irradiated and then reportedly go on to develop malignant changes within the tumor, have you looked at the manner in which the radiation therapy had been administered? We know that excessive dosages of radiations such as 15, or 20,000 rads may be followed by a very high incidence of sarcomatous degeneration, within the irradiated field. We also know that subjects who received small fractions over long periods of time with low doses repeated on multiple occasions also have a high incidence of malignant change. It would be interesting to study such occurrence in patients treated according to present standards of radiotherapy, which are quite different in character.

Dr. Dahlin: I think that generally, in the past, our tumors were treated repetitively and usually with not very high doses at each time, but it's very hard to quantitate the amounts of radiations that were given. Our radiotherapists have been battling that problem and it is probably impossible. I'm glad for your comments, however.

Dr. Brady: In Philadelphia, in looking at patients who have had subsequent malignancy, we found in almost every instance that they have had repetitive courses with small fractions over long periods of time and long intervals between programs, and I think that does significantly increase the risk. In anticipation of this Cancer Seminar, I did look at the results of those patients who have been irradiated for giant-cell tumors by present-day standards. The results are excellent; as a matter of fact, they match any surgical series that one can bring to bear. The data is very limited, but it is not a common tumor and because of the overwhelming influence of surgeons, in their management, very few patients are ever referred to the radiotherapy center for treatment. I would suspect that if one were to irradiate according to conventional fractionation and protraction schedules that we employ today, that we would be able to match any results surgically, with no increase in malignant transformation of the tumor, without arthrodeses and with obvious significant functional improvement.

Dr. Dahlin: This is an interesting thought. A search in the medical literature for information related to radiotherapy, of giant-cell tumors would usually yield confusion. First, there is the question of histologic confirmation; secondly, results of a few months duration are worthless; only long-term follow-up is acceptable. I don't know anything about radiation therapy. Maybe there is a better method than was used in the past. I do know that longterm follow-up is mandatory before you know what is going to happen. Our longest interval, before sarcoma developed in giant-cell tumor was 38 years.

Dr. del Regato: There are, as we see it, two important aspects that deserve the consideration of those who talk and write about it. In the first place, many pathologists have failed to admit their inability to recognize, with any degree of certainty, the malignant potential of these tumors. As a result, a tumor originally called benign and only recognized as malignant after failure of treatment is usually said to have "become malignant." When the treatment given was radiotherapy, adequate or inadequate, radiations were blamed for the "transformation"; if the treatment had been curettement, no one ever blamed the curette as "cancerigenous." It would be more honest, as Dr. Dahlin has done, to admit the limitations of the morphologic diagnosis of these tumors. A second aspect is the one pointed out by Dr. Brady. Radiations may cause cancer in normal bone, but the intensity of delivery, a large amount of radiations in a short time, is the necessary prerequisite for this rare event to take place. It is not often realized that with conventional radiotherapy used years ago, the differential absorption in bone, as compared with soft tissues is of the order of five to one, whereas with the use of supervoltage radiotherapy and cobalt 60 teletherapy, the differential is only as from one and one-half to one. Thus, the intensity of the dose absorbed at the level of the bone was much greater formerly than with present methods.

Dr. Kirsch: St. Petersburg, Fla.: In hyperthyroid persons, one sees a lot of early osteoporosis.

In a pre-existing giant-cell tumor, would this affect the histology? Would the hyperthyroidism alter the histologic pattern of the tumor? Something goes on causing osteoporosis in a hyperthyroid.

Dr. Dahlin: That the giant-cell tumor was produced by the hyperthyroidism or whether it was altered by it, I don't know. I suppose that it might. The only relationship that we know of is that of Brown tumors in hyperparathyroidism, which look something like giant-cell tumors, but I don't think the osteoporosis that you get in hyperthyroidism should affect the giant-cell tumor.

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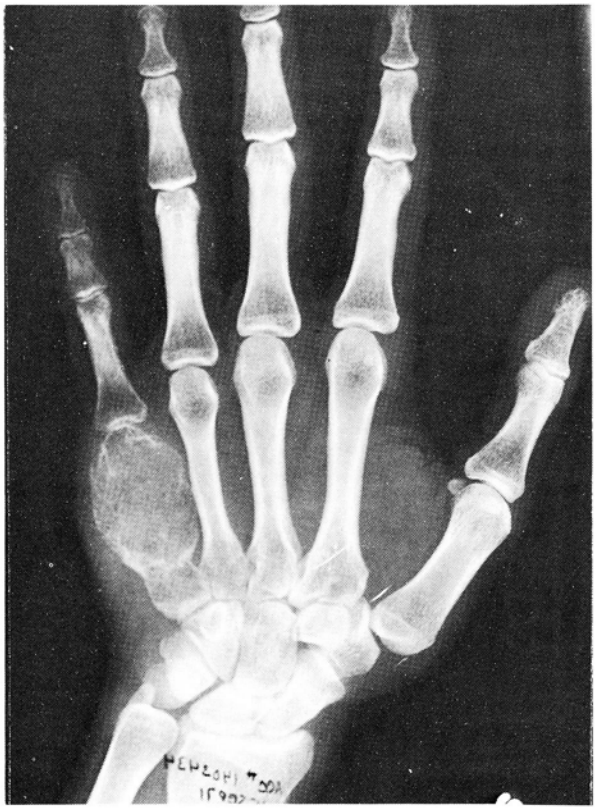
5. Aneurysmatic Cyst of the Fifth Metacarpal Bone

Contributed by **Wm. Martel, M.D.** and **M. R. Abell, M.D.,** Ann Arbor, Michigan

The patient was a 20-year-old woman in September, 1971 when she first noticed a mass on the medial border of the left hand. On examination there was a fixed, very hard, slightly tender tumor arising from the ulnar border of the hand. A laboratory test panel, including serum calcium, phosphorous, phosphatase, etc. showed them all within normal limits.

Dr. Hodes: The only clinical data of significance are the patient's age and the mass noted on the medial border of the hand.

Fig. 1—Cystic lesion of the fifth metacarpal bone with suggestion of loculation.



Three possible diagnoses come to mind, a huge enchondroma, an aneurysmal bone cyst, or a giant cell tumor.

Whereas the hand is not the usual site or origin for giant cell tumors or aneurysmal bone cyst, it is not unusual for an enchondroma.

We are dealing with a cystic lesion which is expanding bone and eroding cortex while new bone is being laid down by an active periosteum with no evidence of the process extending beyond the confines of the cystic lesion. So much of the bone is involved one cannot tell whether it started in the epiphysis or diaphysis. One can be sure, however, it is benign because of the reactive bone surrounding the proximal portion of the bulbous mass. The suggestion of loculation within the mass probably are the remnants of residual cortex.

One feels very confident that the lesion is benign for reasons given above. Differentiating between an aneurysmal bone cyst and a giant cell tumor, however, is the knotty problem. I have seen documented cases of both which look exactly like this which brings into focus the constant argument as to whether or not giant cell tumors and aneurysmal bone cysts are the same. Because most of these lesions in the hand that have traversed the entire shaft in this fashion have been proven to be giant cell tumors, I shall call this a giant cell tumor rather than an aneurysmal bone cyst.

Dr. Hodes' impression: Giant-Cell Tumor

Radiologic Impressions Submitted:

Giant-cell tumor	48
Aneurysmal cyst	48
Enchondroma	44
Fibrous dysplasia	05
Chondroblastoma	05
Osteoblastoma	05
Others	14

Dr. Hodes: I would not hazard fibrous dysplasia; we have monostotic fibrous dysplasia but

I usually steer away from that diagnosis, unless I'm forced into it. The chondroblastomas and osteoblastomas are rare lesions. Chondroblastomas usually have much more bone reaction than this. They tend to be more juxtaepiphyseal. I'm not sure about the osteoblastoma; I'd want to consider that. I think this is a giant-cell tumor.

Dr. del Regato: Drs. E. Braukman and E. Schulz of St. Petersburg, offered an impression of giant-cell tumor. Dr. Francisco Convers, of Bogota, Columbia, offered chondromyxoid fibroma. Dr. B. Felson, of Cincinnati, said that it was one or the other of these two. Dr. Alan Wolson, of Ann Arbor, hesitated between giant-cell tumor and aneurysmal cyst. Dr. J. Maxey Dell, of Gainesville, Florida, felt that the lesion was too dense for a giant-cell tumor and preferred chondroblastoma.

The University of Missouri radiodiagnostic computer diagnosed chondromyxoid fibroma.

Operative findings: On October 15th, 1971 the fifth left metacarpal bone was excised, preserving the tendinous structure; it was replaced by a shortened 4th metatarsal bone from the right foot. The excised bone contained an ovoid lesion 5x3x3 cm which on cut section was spongy with several cystic areas, the largest 2.5 cm in diameter.

Dr. Dahlin: The roentgenogram indicates a central rarefying and rather markedly expansile lesion of the metacarpal bone. Histologically there are no evidences of malignancy in the form of nuclear hyperchromatism or anaplasia. The lesion exhibits a prominent component of vascular spaces which measure up to 1.5 cm. in diameter. Many of these are filled with blood. The spaces contain no recognizable lining. Between the spaces is a variable picture. In some zones one sees edematous fibroblastic connective tissue separating the spaces. In some areas the mononuclear stromal cells form aggregates and have developed into benign multinucleated cells so that in these zones the appearance is suggestive of giant cell tumor. In many zones the fibroblastic connective tissue has undergone metaplasia and produced chondroid and even osteoid matrix. In turn the trabeculae thus formed are mantled by and contain mononuclear cells. There is no evidence in the section of any underlying nameable disease such as fibroma or chondroblastoma.

The differential diagnosis includes, in addition to aneurysmal bone cyst, any of the underlying diseases that can produce an aneurysmal bone cyst-like response. None are present in the material submitted and I would expect none. Our policy has been that if an underlying nameable

Fig. 2—Magnified view of one end of the surgical specimen.

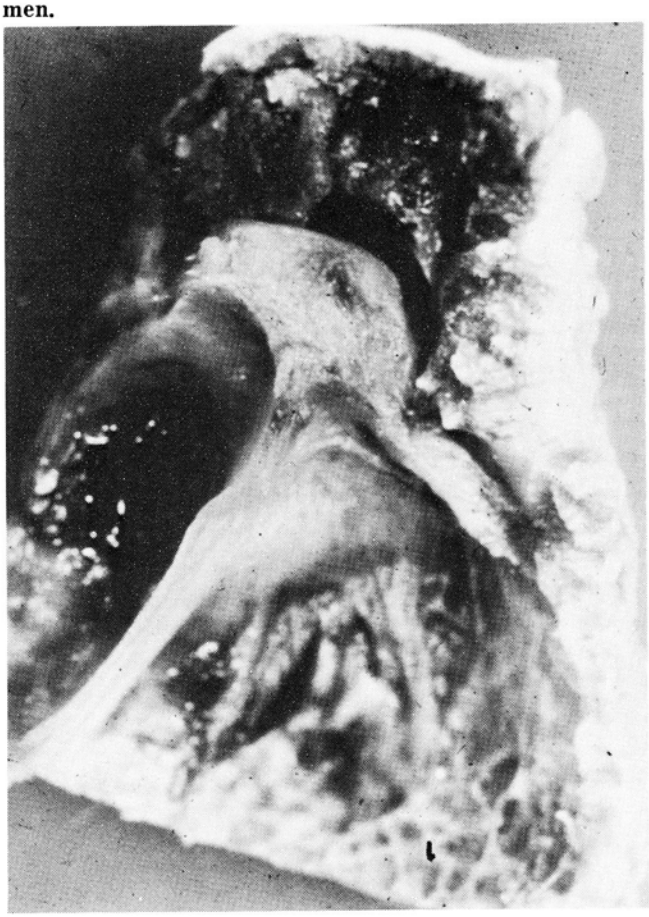
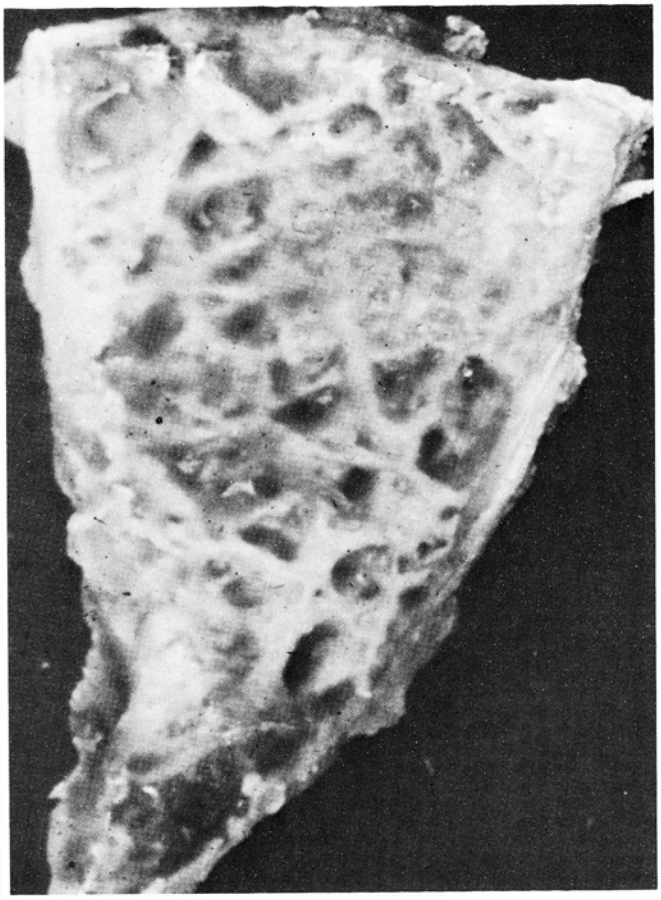


Fig. 3—Spongy appearance of cross section of lesion.



process such as fibrous dysplasia or chondroblastoma or even osteogenic sarcoma is present such diagnostic material is "trump." An aneurysmal cyst-like response is considered to be secondary. The differential diagnosis must, of course, include any benign expansile lesion of a small bone and one should think of chondroma, chondroblastoma, chondromyxoid fibroma, giant cell tumor and possibly even more unusual things.

Dr. Dahlin's Diagnosis: Aneurysmal Bone Cyst

Histopathologic Diagnoses Submitted:

Aneurysmal cyst	82
Osteitis fibrosa cystica	08
Giant-cell tumor	07
Others	06

Dr. Dahlin: Osteitis fibrosa cystica isn't really a diagnosis. It's sort of like saying, the patient has fever. If this were a giant-cell tumor, it's so completely cystic that it's impossible for me to determine that it was ever a giant-cell tumor.

Dr. del Regato: In various languages and only with minor variations in spelling, the experts diagnosed an aneurysmatic cyst. Dr. S. Spanier of Gainesville, Fla. felt uncomfortable about intravascular plugs of "tumor." Dr. M. McGavran, of Hershey, Pennsylvania, preferred the old designation of osteitis fibrosa cystica. Dr. L. V. Ackerman of Stony Brook felt that hyperparathyroidism had to be ruled out. Dr. John B. Frerichs, of El Paso (west of Pecos), Texas, wondered if there is a more appropriate label than aneurysmal bone cyst.

Dr. Lent C. Johnson, AFIP, Washington, D.C., wrote: I saw this case previously. The lesion was a cavity containing nothing and surrounded by typical giant-cell tumor. This Cancer Seminar slide has few cystic spaces; most of it is solid. Aneurysmal bone cyst is a state of grace enjoyed by many different lesions, not a lesion in its own right (Jaffe, Biesecker). Any bone lesion may develop degenerative changes and become cystic. The cyst is not to be used in naming it, but the cells from which the cyst arose. Failure to observe this general rule of pathology leads to such atrocities as "aneurysmal bone cyst."

Subsequent History: Patient has been reported to have had a good functional result and has no complaints.

Dr. del Regato: When I was in training, we used to treat, variously, a number of bone tumors

Fig. 4—Vascular spaces without recognizable lining separated by fibroblastic tissue which in some areas suggests a giant-cell tumor (x 250).

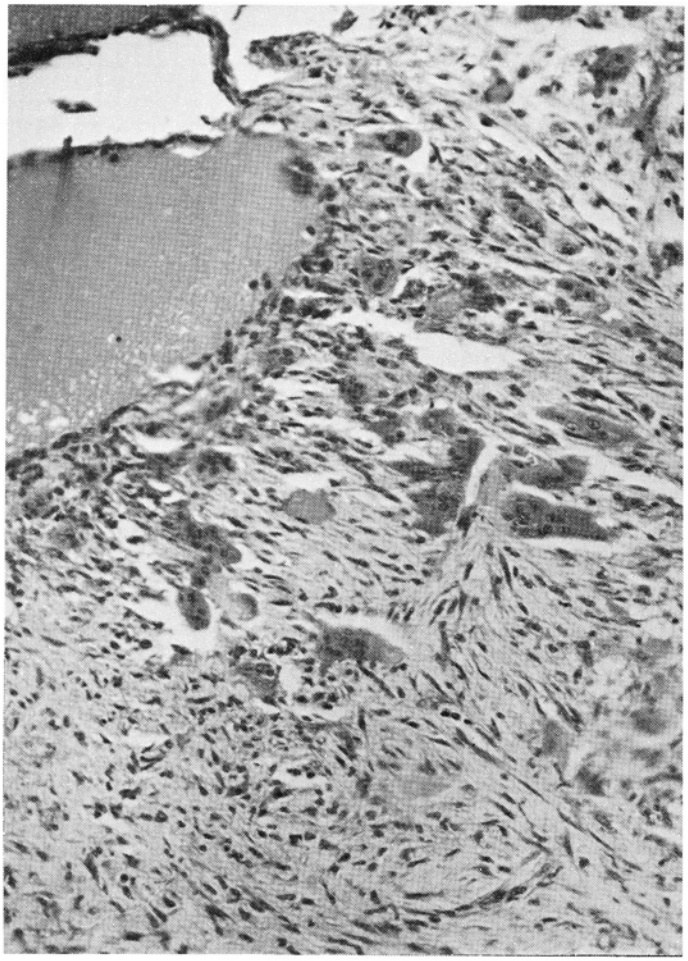
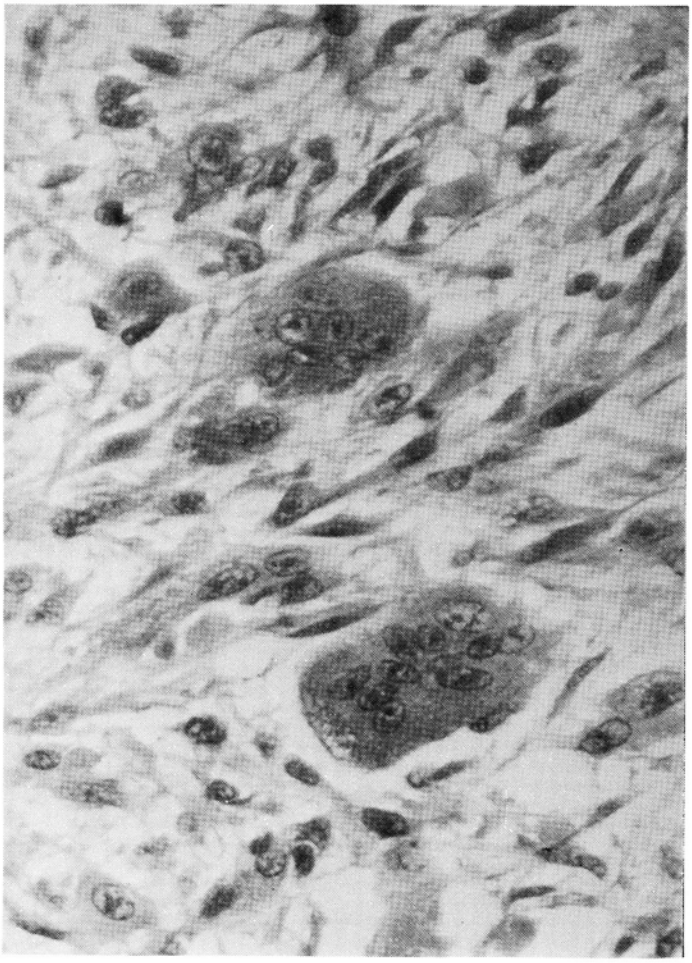


Fig. 5—Detail of giant-cells (x 400).



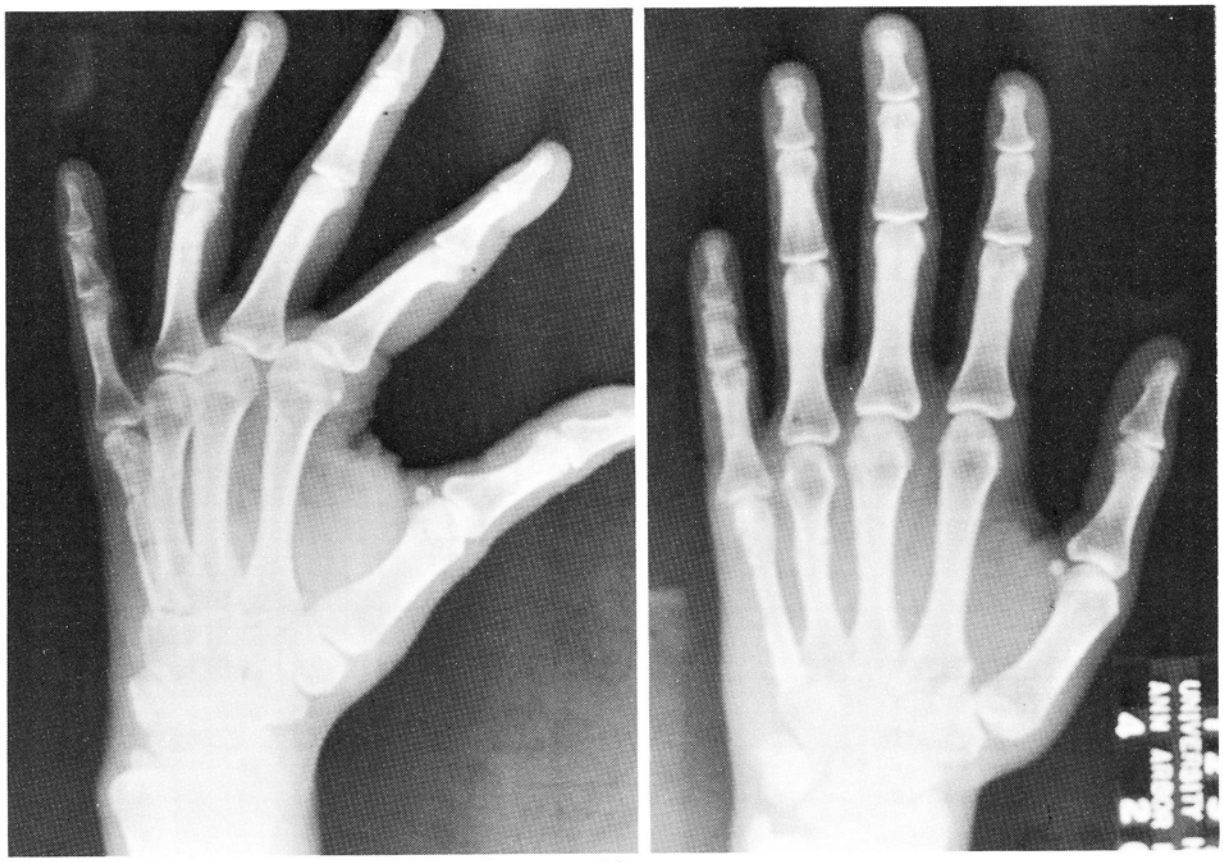
which were then diagnosed as giant-cell tumors. Some 25 years ago, the concept was sprung that those which occurred in patients under 20 years of age could not be giant-cell tumors, that many of those were aneurysmal cysts. The discussion of this Cancer Seminar case, sent by Dr. Lent Johnson, is very edifying, if retrogressive, in view of the patient's age.

Dr. Sim: From the clinical standpoint in this patient with an extensive trabeculated lytic lesion involving the metacarpal, the differential diagnosis would include the entire broad spectrum of benign expansile lesions of a small bone including chondroma and giant cell tumor. From the therapeutic standpoint, the treatment is basically the same. For small expansile benign lesions involving the metacarpal, the small bones lend themselves to effective treatment with curettage and restoration of the integrity of the bone with iliac bone grafts. In a lesion such as this which is much more extensive, our therapeutic approach would necessitate en bloc resection of the entire lesion and the involved portion of the metacarpal. The reconstruction would be carried out in one of two ways, if the articular surface could be preserved without jeopardizing the outcome then the osseous integrity could be restored with a block of iliac bone graft preserving the joint. This would be the simpler procedure. The other approach which is necessary in this case because of the extensiveness of the lesion and involvement of the articular surface would be to deliver the entire metacarpal bone including the joint to the pathologists in an en bloc resection. We would then use a metatarsal bone in the reconstruction. One might expect approximately 30 degrees of flexion and in a few similar cases we have handled, a good functional result has been obtained. On the other hand, if these techniques are not successful, then a ray resection would give an adequately functioning hand with a good cosmetic result.

Dr. James J. Biemer, Tampa, Fla.: Would Dr. Dahlin expand his comments regarding non-ossifying fibroma?

Dr. Dahlin: We use the term metaphyseal fibrous defect as sort of synonymous with non-ossifying fibroma. I think it is quite a different lesion than this, although the location of aneurysmal bone cyst is closer to what we call a non-ossifying fibroma than any other disease is. A simple bone cyst is a growth disturbance; if you get curettings from it the histiology can overlap what we call aneurysmal bone cyst. All I can do is recognize that such a problem exists. Whether aneurysmal bone cyst is a reasonable diagnosis, I don't really know. I think it is a recognizable entity but such things as giant-cell granulomas of the jaw bones have areas that are similar to what we call aneurysmal bone cyst. Dr. Levy of Philadelphia showed a group of post-traumatic lesions of bone that are similar in many respects to what we call aneurysmal bone cyst. I have seen two or three

Fig. 6—Follow-up roentgenogram showing replacement of fifth metarcarpal by a pared metatarsal.



lesions where it looked just like a myositis ossificans in the bone, believe it or not. It seems to me that anything that insults a bone may result in an alteration which most of the time we recognize in long bones as aneurysmal bone cysts, but it's probably just one part of the spectrum of reaction of response to injury or trauma of some sort.

Dr. Azar: I had the occasion of examining a huge aneurysmal bone cyst, in 1971, at the University of Kansas, a beautiful one radiographically, and an aneurysmal bone cyst histologically; it was evacuated twice and a beautiful nodule developed in the soft tissues along the scar, which was a benign giant-cell tumor. I mention this because I am quite aware of the constant dialogue about relationships of aneurysmal bone cyst and giant-cell tumor found in the literature. I wonder whether Dr. Dahlin has had a similar experience; maybe our interpretation was all wrong.

Dr. Dahlin: A case like that is to be expected. I think that it was a giant-cell tumor that had so much cystification that it was very difficult or impossible to diagnose. We had a large lesion of the sacrum recently at St. Mary's in Rochester, and I called it a giant-cell tumor, although everyone else thought it was an aneurysmal bone cyst. I guess you use an effervescent sixth sense to know that it's going to recur and that it is likely to be aggressive as a real tumor should be. All I can say is that such problems do come up where it's very difficult to know whether the lesion at hand is really a giant cell tumor. The rule that we use—it seems valid—is that if any of the solid area looks like a giant-cell tumor ought to look, then the recurrence may be just a solid meaty tumor and it really is a giant-cell tumor. I think it should be emphasized that if you use radiographic guidance, this kind of problem case is unusual, but yet it does occur.

Dr. Perez Mesa: There would be a possibility then, rather than calling it one or the other, that we should call it S.O.G., State of Grace.

Dr. Hodes: May I ask, Dr. Sim, has angiography helped you any in differentiating between the aneurysmal bone cyst and giant-cell tumors?

Dr. Sim: No, we have not been enthusiastic about arteriograms or angiograms in differentiating these lesions because we have to biopsy them anyway, but we are using it in cases in order to plan surgery, for planning of the surgical approach—the approach to the vessels. I'd like to have your comment on the use of arteriograms.

Dr. Hodes: With reference to the osteomas, I don't believe that as a group they are very difficult, and certainly the angiogram will help you very considerably, showing you a tumor blush. I wonder whether we should use it in this problem. Dr. Dahlin has said that the aneurysmal cyst is a blown-out lesion radiographically. I was confused before, but I'm confused at a much higher level now. We had a rib lesion (Case No. 2) that I called an aneurysmal bone cyst. It was blown way out, and yet we called it a fibrous dysplasia. Then we had that distal end of the femur, the one film which was blown-out; I thought it was a giant-cell tumor; I was very fortunate because that is what it was. But now we come to this hand. I should have remembered the age of the patient; I should have remembered that this portion of the hand is constantly being traumatized. I should have made the diagnosis. But I'm a little bit afraid of this blown-out characteristic because I see it in so many other aggressive lesions. I hope that at the Mayo Clinic you will do a lot more angiography because I think it may give us a clue in the differential diagnosis. I'm aware it helps you in planning your surgical technique, but I just wonder, in a problematical case, particularly in a malignant giant-cell tumor, you may be able to see the peculiar vascularity that characterizes malignant tumors.

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6. Giant-Cell Tumor of the Head of the Femur

Contributed by **Wm. Martel, M.D.** and **M. R. Abell, M.D.**, Ann Arbor, Michigan

The patient was a 25-year-old woman in January, 1968 when she gave a history of progressive pain in the right hip which, six months previously, had led to the discovery of a lesion of the neck of the femur. Curettage and packing with bone chips was followed by progressive recurrence of pain, painful gait and limping. Examination revealed only limitation of movement due to pain. The alkaline phosphatase, calcium, phosphorus, SGOT and SGPT were all within normal limits.

Dr. Hodes: The clinical history of progressive pain in a twenty-five year old woman which was operated upon six months previously is a little help unless we bear in mind the patient's age.

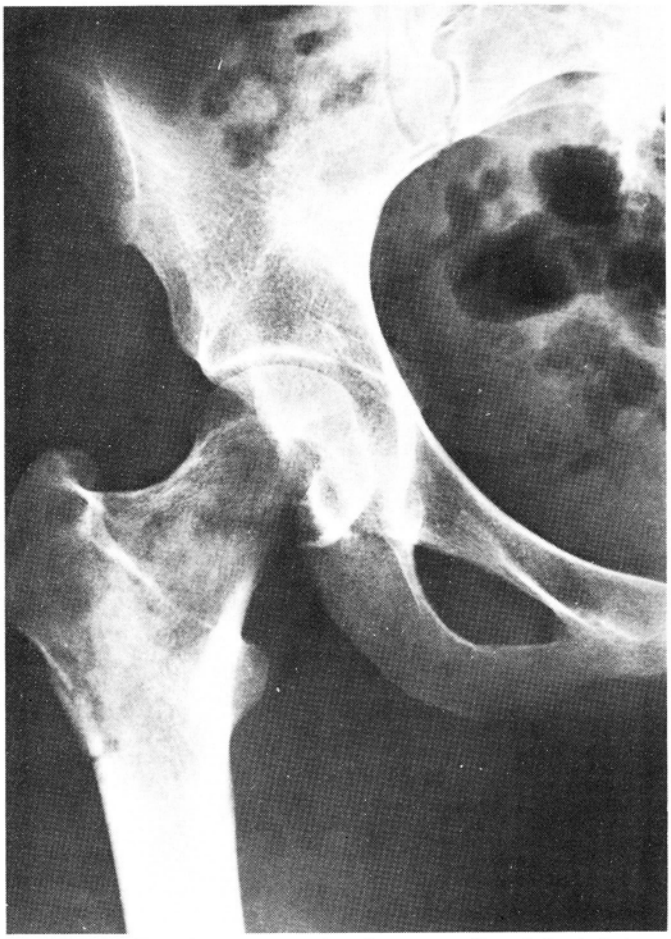


Fig. 1—Roentgenogram showing operative defects below greater trochanter. The lesion extends into the femoral head.

We are told the lesion was packed with bone chips very few of which can be determined in the current examination. All one sees is the operative defect below the greater trochanter. This lesion traverses the entire width of the neck of the femur and extends well into the femoral head. Its proximal margin is sharply delineated by a thin zone of reactive bone. The rather broad transitional area along the distal margin of the lytic lesion is probably the result of the surgical procedure and cannot be interpreted as a meaningful finding. I am inclined, therefore, to consider the proximal margin of the lytic lesion alone to be significant.

I am not sure that both exposures were made at the same time. In the lateral projection there is a defect along the superior margin which looks like an infraction or mollecular fracture. It is in this exposure alone that one can see bone chips.

Despite the fact that this is not an eccentric or asymmetrical bone defect, I am persuaded by its presence in the juxta-articular portion of the bone and the patient's age to consider it a giant cell tumor. An ordinary bone cyst would not have caused this degree of osteolysis plus the cortical thinning. The position would be unusual for an ordinary bone cyst but they do occur here. Actually, they lie more in the diaphyseal portion of the bone.

In the patient's original roentgenograms, we were impressed by the fact that the bone seemed somewhat decreased in density. Were we sure of this and could see manifestations of metabolic bone disease in the hands or spine, one would have to consider the cystic lesions sometimes seen in hyperparathyroidism. We are told nothing about the patient's electrolytes.

The evidence, therefore, leads one to conclude that this benign bone lesion must be a giant cell tumor.

Dr. Hodes' Impression: Giant-cell Tumor

Radiologic Impressions Submitted

Giant-cell Tumor	38
Aneurysmal cyst	24
Osteosarcoma	14
Fibrosarcoma	13
Chondrosarcoma	13
Malignant lymphoma	10
Osteomyelitis	07
Eosinophilic granuloma	04
Quien sabe que horror!	01
14 Others	24

Dr. Hodes: I saw nothing here that made me think of an osteosarcoma. Fibrosarcomas in this age group are rather unusual and furthermore, it was an osteolytic, cystic type of lesion. There was no calcified chondroid. The beautiful manner in which you can see a transitional zone around the proximal limb militated against a diagnosis of a malignant lesion. Where osteomyelitis would come along in here, I cannot see, because there is no cortical reaction at all, there is no bone response. Eosinophilic granuloma never occurred to me but that might not be a bad idea, because it could occur; the patient's a little out of the age group, but that does not militate against it. I sort of like that diagnosis but, statistically it doesn't stand.

Dr. del Regato: Dr. M. Valette, of Paris, suggested hyperparathyroidism. Dr. R. O. Bretz, of Long Beach, offered bone cyst or giant-cell tumor. Dr. M. Childress, of Ann Arbor, preferred fibrosarcoma, Dr. A. W. Finestone, of Clifton Forge, Virginia, wavered between giant-cell tumor and fibrosarcoma. Dr. E. Hernandez-Romero of Mexico City, offered an impression of benign chondroblastoma, and Dr. M. I. Chavez-Abrego, also of Mexico, preferred osteosarcoma.

The University of Missouri radiodiagnostic computer diagnosed fibrosarcoma.

Operative findings: On February 6th, 1968, a resection of the femoral head was followed by a "colona" arthroplasty. A reddish-brown mass occupied much of the anterior and medial portions of the excised head of the femur; it appeared to break through the cartilage anteriorly and was very close to the line of resection.

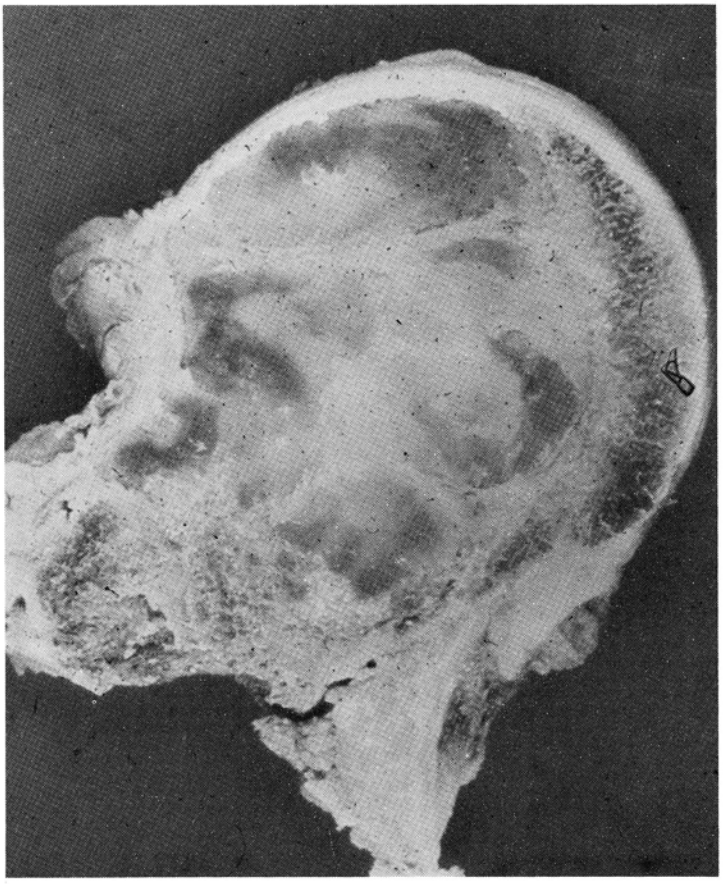
Dr. Dahlin: In this case the roentgenographic picture provided may be confusing but the microscopic section indicates the tumor extends to the

articular cartilage. This fact plus the patient's being 25 years of age make giant cell tumor a likely possibility. The dominant element again is a proliferating mononuclear cell. Mitoses are not difficult to find and one might become alarmed because some of the mononuclear cells are larger than the average and have rather prominent nucleoli. They are, however, not significantly worse than some of the nuclei within the multinucleated benign giant cells present. This rule of comparing the mononuclear cell nuclei with the nuclei within the multinucleated cells helps in assessing that the lesion is benign. Areas within this tumor show considerable osteoid production but again the trabeculae are mantled by benign appearing osteoblasts. At least half of giant cell tumors contain such osteoid. In other fields rather marked fibrogenesis has developed. Neither the osteoid or fibrous tissue-containing zones are diagnostic. The same comments regarding inability to grade giant cell tumor apply to this case.

Differential diagnosis would probably include malignant giant cell tumor but I do not believe that the individual mononuclear cells are anaplastic enough to support the diagnosis of sarcoma.

My diagnostic conclusion is that this is a giant cell tumor. It is somewhat more hazardous to the patient than usual because of its location at the upper end of the femur.

Fig. 2—Surgical specimen of femoral head containing loculated lesion which extends to line of excision.



Dr. Dahlin's Diagnosis: Giant-Cell Tumor

Histopathologic Diagnoses Submitted

Giant-cell tumor	85
Brown tumor	06
Others	08

Dr. Dahlin: I think this lesion is too cellular for a Brown tumor. Hyperparathyroidism—it occurs exactly where the giant-cell tumor ought to be. Everything fits for giant-cell tumor, including the histology. We haven't been trapped into mistaking hyperparathyroidism for giant-cell tumor. I think that when anything is a little bit off-color, one should think about hyperparathyroidism as the cause; but what you must first think is giant-cell tumor.

Dr. del Regato: Rather overwhelmingly, our experts agreed on a diagnosis of giant-cell tumor. A few indicated that Brown tumor should be ruled-out; others dared to classify the case as malignant. One correspondent specifically inquired if Dr. Dahlin had changed his mind about grading these tumors.

Dr. Lent C. Johnson, AFIP, Washington, D.C., wrote: This is a giant-cell tumor. Areas of spindle cells are not enough to change this diagnosis. There are also areas of dense collagen scarring. Progressive scarring of this sort carries with it the virtual certainty of eventual sarcoma, whether it occurs spontaneously, in an incompletely removed lesion, or follows x-ray therapy. If this material is from the site of previous graft, no special interpretation is needed.

Subsequent History: On November 14th, 1974, the patient was last seen. There is occasional pain and some disturbance of gait, but no radiographic change since operation, nor any other indication of recurrence.

Dr. Sim: From the clinical standpoint, a large recurrent giant cell tumor extending to the articular surface in the femoral head and distally into the trochanteric area poses a tremendous therapeutic challenge to the surgeon. In lesions such as this, the surgeon is confronted with two problems: first is cure of the disease and second is to preserve or restore function in the hip joint. In benign lesions such as this, our approach has been to control the disease by excising the tumor or curettage and restoring the integrity of the femoral head and proximal femur with iliac bone grafts. This case shows, I think, one of the pitfalls involved in treatment of these osseous lesions. Certainly the initial curettage appeared to be inadequate because the window in the bone was no more than an inch long. Adequate treatment of these lesions requires complete exteriorization. We would have been much more radical removing the entire greater trochanter to allow direct access and complete exteriorization of the tumor cavity. This would give us a better chance of success without later recurrence. In such an aggressive recurrent lesion extending to the femoral head and as the lateral x-rays show it ex-

tends directly to the articular surface and erodes the cortex, I think it is too late for another attempt to preserve joint function with curettage and grafting. In such recurrent extensive benign lesions compromising the integrity of the hip joint, radical en bloc resection of the proximal femur and joint is necessary. The treatment of choice in this case would be a segmental resection of the femoral head and neck. With improvements in reconstructive techniques in orthopedic surgery utilizing custom proximal femur implants and total joint replacement principle, we can now restore the integrity of the proximal femur and preserve the physiological function of the hip joint. There is a new breed of oncological surgeons who also have an interest in reconstructive total joint replacement. Application of these recent advances in orthopedic surgery to the area of orthopedic oncology has been very rewarding.

Dr. del Regato: Some repetitions continue to be heard, as the statement that radiotherapy causes some of these tumors to "become" malignant. It should be obvious that the morphologist cannot often diagnose with certainty the malignant potential of giant-cell tumors. When they recur after radiotherapy, radiations are blamed. The same occurs after curettement, but the curette is never blamed for the transformation. Some of the authorities' concepts seem to be of the same vintage as is their repeated references to "x-rays" and "x-ray therapy"!

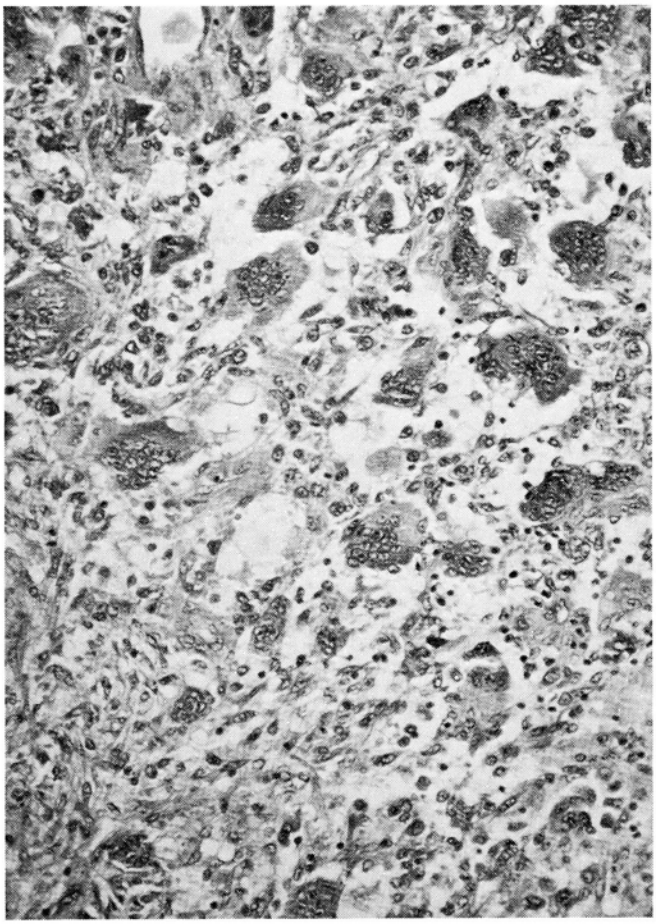


Figure 3—Proliferating mononuclear cells which are not visibly malignant.

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7. Fibroblastic Osteosarcoma of the Distal Femur

Contributed by **H. D. Dorfman, M.D.,** Baltimore, Maryland

The patient was a 40-year-old woman in April, 1971, when she complained of pain and swelling of the left knee of several months duration; aspirations of fluid from the area had brought no relief. On examination, there was a tender, fluctuant mass on the medial aspect of the left knee. There was a slight elevation of alkaline phosphatase.

Dr. Hodes: The clinical findings include pain, swelling, joint fluid, all of several months duration in a forty-year-old woman.

The films we received were magnification views of the distal end of the femur, one in the sagittal projection and a second in an oblique projection. We did not see any true lateral projection of the knee. I doubt whether this would have given us more information.

This metaphyseal lesion primarily involves the medullary portion of the bone which it has invaded in eccentric fashion. It is not the usual asymmetrical juxta-articular osteolytic process that characterizes giant cell tumors. It is an aggressive lesion which has broken through cortex with some periosteal reaction. The transitional areas within the medullary canal are very vague. Irregular densities within the central portion of the bone in some respects suggest calcified chondroid matrix. Perifocal soft tissue swelling is obvious which looks more like inflammatory reaction rather than mass due to extension of the

tumor beyond the bone; posteriorly, however, I am confident that the tumor mass has broken through the cortex eroding and displacing it.

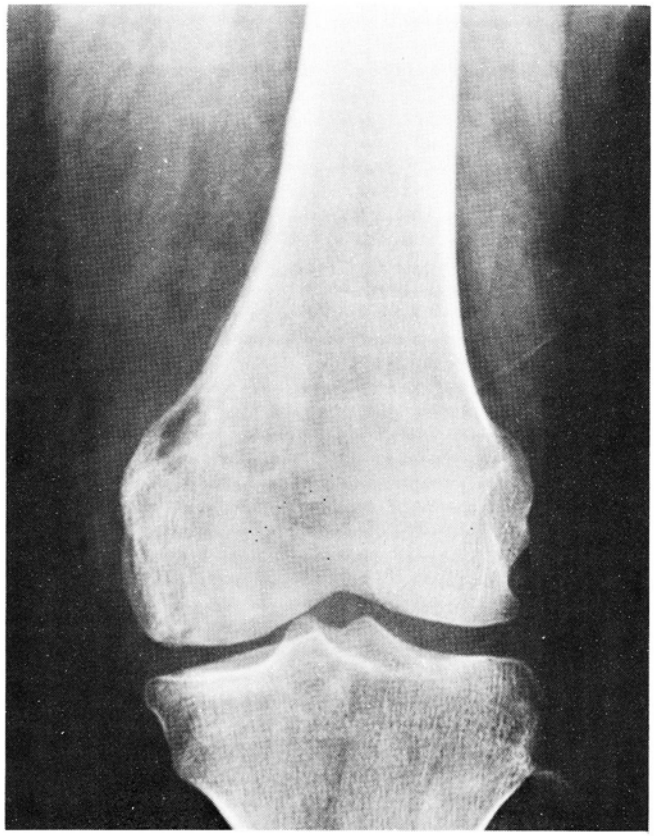
This looks like a malignant tumor. The pain and location and even the patient's age are consonant with a centrally placed chondrosarcoma. The peculiar calcifications are not unlike calcified chondroid matrix. In some respects, however, the latter suggest sequestration, the large density seen in the oblique projection in the proximal half of the osteolytic process particularly. The presence of sequestrum-like foci in osteolytic lesions is one of the hallmarks of fibrosarcoma.

Mention is made that this patient's alkaline phosphatase was slightly elevated. There is some evidence of new bone formation in the tumor which could explain this finding. But the tumor is not a bone forming tumor; it is more a bone destroying lesion.

It has been my experience that when one has difficulty categorizing a bone tumor, one should always think of fibrosarcoma.

More recently the pathologists have been describing fibrous histiocytomas which radiologically have simulated atypical giant cell tumors and fibrosarcomas. I have found the diagnosis creeping more and more into focus particularly in patients with atypical giant cell tumors, fibrosarcomas and in lesions I thought were malignant tendon sheath tumors.

Fig. 1—Metaphyseal lesion of the femur involving primarily the medullary portion with irregular densities within the central portion of the bone.



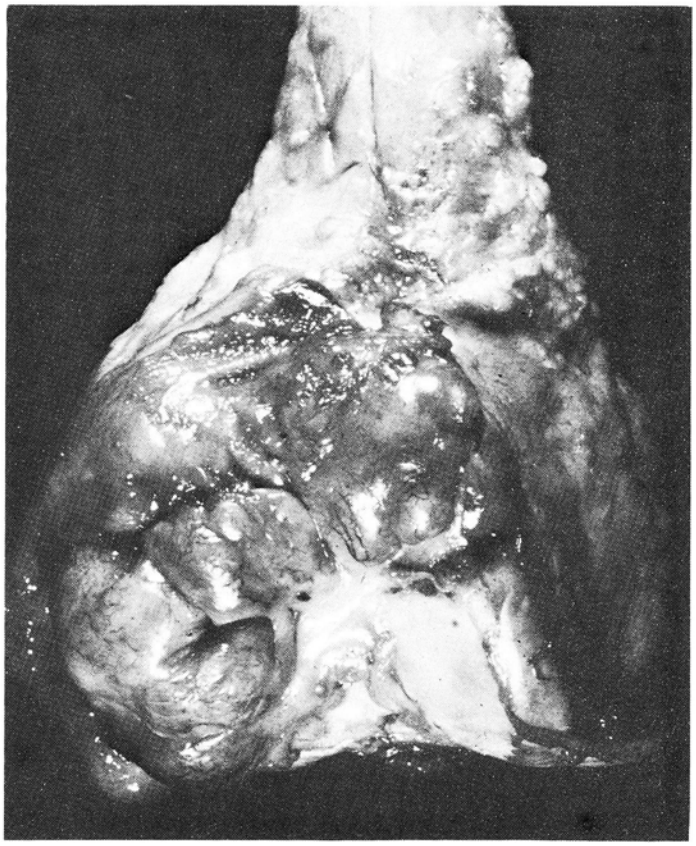


Fig. 2—Gross appearance of surgical specimen.

Dr. Hodes' Impression: Fibrosarcoma

Radiologic Impressions Submitted

Osteomyelitis	41
Osteosarcoma	21
Fibrosarcoma	20
Reticulum-cell sarcoma	20
Synovial sarcoma	15
Chondrosarcoma	06
Metastatic tumor	05
Others	21

Dr. Hodes: I have given my reasons against osteomyelitis. I can see reasons for thinking of the possibility of osteosarcoma; they obviously thought there was a malignant lesion, but there was no true tumor osteoid or calcification; it did not look like neoplastic bone to me. Fibrosarcoma or reticulum-cell sarcoma would be more destructive than this; you would probably have more of a soft tissue component also. Synovial sarcoma—I can't gainsay; I never thought of it—I still don't like the diagnosis. Synovial sarcomas are somewhat more destructive; they may extend across the joint actually, although most of them do not. The patient is only 40 years old, so that's why I did not think of metastatic lesion.

Dr. del Regato: Dr. M. Viamonte, of Miami, Dr. M. Corte-Real, of Lisbon, and Dr. J. Cordillo of Moroleon, Mexico, suggested fibrosarcoma. Drs. J. Ceballos and G. Moreno, both from Mexico City, offered osteosarcoma.

The University of Missouri radiodiagnostic computer diagnosed reticulum-cell sarcoma.

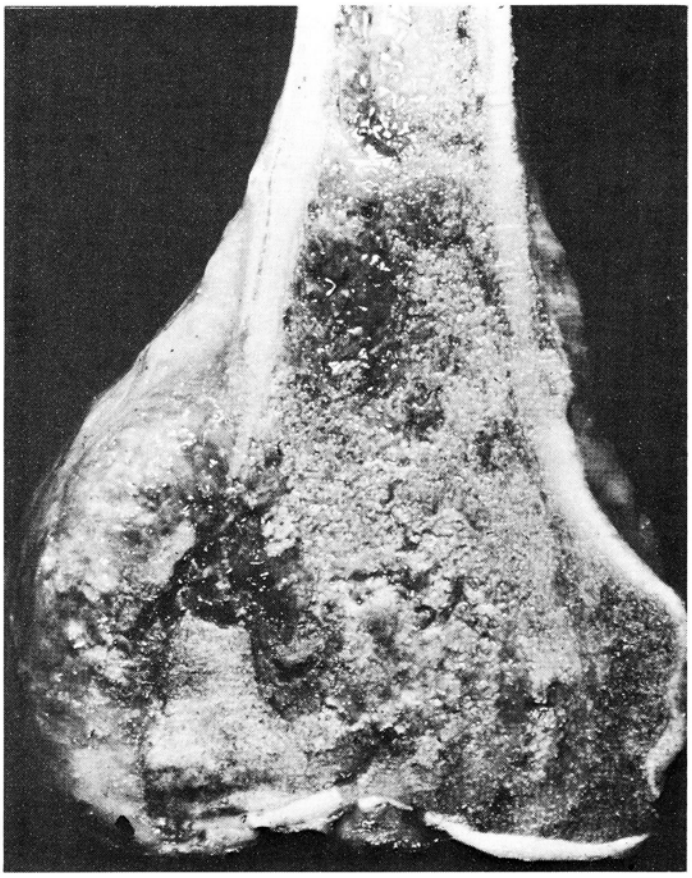


Fig. 3—Cross section of lesion of tumor extending through the medial condyle.

Operative Findings: Following initial biopsy, on October 8th, 1971, a high thigh amputation was carried out. The tumor involved the distal 9 cm of the femur, extending medially through the cortex of the medial condyle and at the intercondylar notch. On cut section the tumor had a gray-red flesh appearance. There was periosteal elevation in the adjacent proximal area to the tumor. Sections of the soft tissues and popliteal lymph nodes revealed no tumor. The areas of increased bone density were non-neoplastic.

Dr. Dahlin: Roentgenographically my colleague again considered this patient to have a malignant tumor. Microscopically the dominant element is spindle cell or fibrosarcoma. In most areas these spindle cells are producing abundant collagen. In the more anaplastic, grade 4, areas they appear to have lost the capability of doing this. In some zones there is a suggestion of storiform pattern and a generous sprinkling of chronic inflammatory cells. These features suggest malignant fibrous histiocytoma as a designation and further suggest according to the work of Spanier that lytic, that is non-ossified metastases, in this case might be radiosensitive. My colleague, Dr. E. H. Soule, does not feel this tumor has the pattern of malignant fibrous histiocytoma. Within the bony substance, the spindle shaped cells of this tumor appear to be producing osteoid. In fact there is one area within the bone itself where a degenerating focus of cartilaginous tumor is present suggesting that there might have been an indolent cartilaginous precursor. Evidence for such a genesis is too nebulous to more than suggest, however.

The differential diagnosis in this case includes malignant fibrous histiocytoma which I believe it is not because there is definite osteoid production and bone production by tumor cells in some zones. Ordinary fibrosarcoma is also a possibility but again such a diagnosis is negated by the areas in which malignant cells are producing osteoid and bone. Fibrosarcoma and fibroblastic osteosarcoma are very closely related as to histology and as to prognosis.

Dr. Dahlin's Diagnosis: Fibroblastic Osteosarcoma

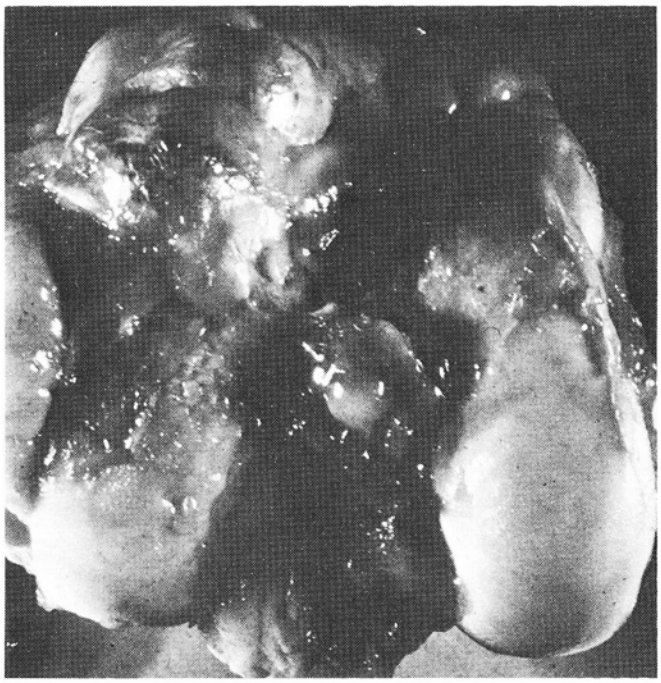
Histopathologic Diagnoses Submitted:

Fibrosarcoma	73
Osteosarcoma	06
Malig. fibrous histiocytoma	06
Others	21

Dr. Dahlin: Most participants did not believe that the bone was a product of the tumor, and I think they are right.

Dr. del Regato: Most of our correspondents made a categorical diagnosis of fibrosarcoma. Dr. H. D. Dorfman, of Baltimore, whose case this was, pointed at the unusual extension to the knee joint with synovial infiltration and effusion; he thought that a differential diagnosis has to be made with malignant fibrous histiocytoma. Dr. H. A. Sissons, of London, wrote that the case does not have the feature of histiocytoma, but found the intense plasma-cell reaction interest-

Fig. 4—Extension at intercondylar notch.



ing, possibly betraying "immune reaction." Dr. Carlo Sirtori, of Milan, also made a diagnosis of fibrosarcoma and in reference to these diagnostic problems went on to quote Shakespeare, ". . . the native hue of resolution—is sicklied over with the pale cast of thought". In present day parlance: your think might only sap your hunch!

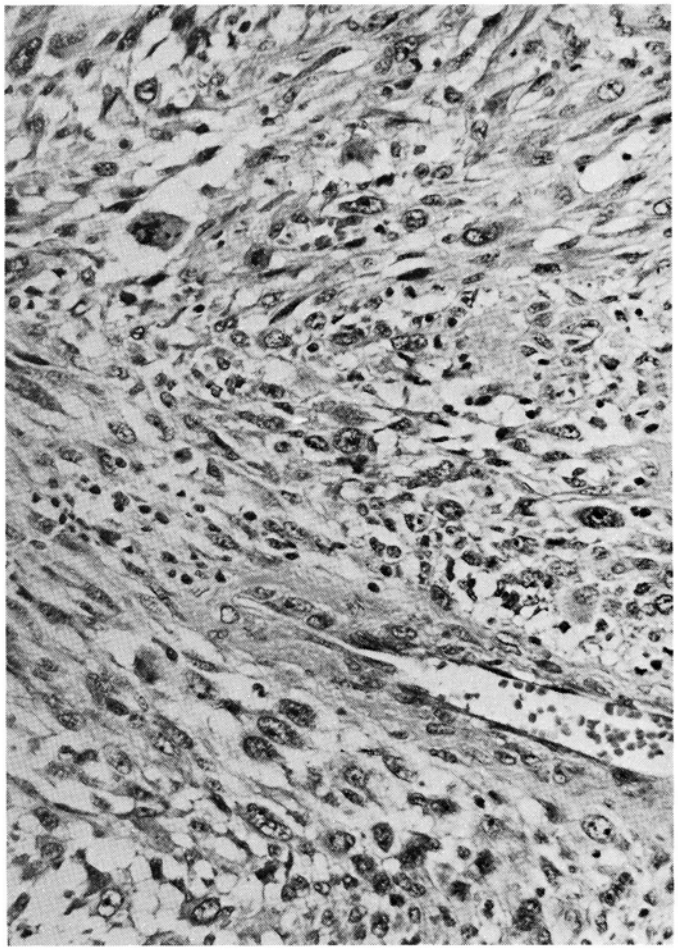
Dr. Lent C. Johnson, AFIP, Washington, D.C., wrote: This is a malignant spindle-cell tumor. It has been customary to call such lesions fibrosarcomas. The cancellous bone is sclerotic due to reinforcement of trabeculae by non-neoplastic bone. Between the trabeculae there are malignant spindle cells and malignant "xanthoma" cells. A new notion and a new term, fibrous histiocytoma, have been introduced recently; they are based upon the assumption that xanthoma cells are histiocytes filled with fat. This is not true. The non-ossifying fibroma or, fibroxanthoma, as we prefer to call it, develops where cancellous bone gives way to fatty marrow. The malignant form of this lesion should be called malignant fibroxanthoma: that is my interpretation of this case.

Subsequent History: Following amputation, the patient was apparently well for 2½ years. In February, 1974, she developed left inguinal metastases, biopsy of which revealed an identical tumor to the one found in the femur. Shortly afterwards she was found to have bilateral pulmonary metastases and on August 2nd, 1974, she expired.

Dr. Sim: From the clinical standpoint this 40 year old female represents one of the common pitfalls in the management of osteogenic sarcoma. In this case there is a long delay in diagnosis and the first hurdle is the recognition that an osseous lesion exists. Preoperatively we would do an extensive workup to exclude metastatic disease. One of the problems in management of this disease is the presence of occult metastatic spread and an attempt must be made to increase our diagnostic accuracy in detecting occult metastatic lesions. This includes whole lung tomography, skeletal surveys and bone scans. As far as treatment of these radioresistant lesions, radical ablative surgery is required with amputation or disarticulation as needed. The survival rate is 20%. This means that 80% are going to die of their disease. It is obvious that we have to find other methods of increasing the actual survival of these patients. This is the biggest problem that we are faced with today. We all realize that in the past 50 years little or no pro-

Fig. 5—Spindle-cell appearance predominant in tumor (x 250).

Fig. 6—Areas suggesting inflammatory element.



gress has been made in increasing the survival rate of these tumors. In analyzing the 20% of patients that survive of their disease it becomes obvious that we have gone as far as we can with amputation surgery and that there are certain host immunological factors that play a large role in determining which patients will survive. Because of this aspect of our investigation, patients with osteogenic sarcoma undergo a complete immunosurveillance profile monitoring. This includes delay hypersentivity skin testing, humoral cytotoxicity and lymphocyte transformation studies. It does appear that this does have significance in which patients will ultimately survive or die of their disease. Our humoral cytotoxic indices indicated that in osteogenic sarcoma 94% of patients with positive humoral cytotoxic indices remain disease free for six months and 75% of those with negative indices died or developed metastatic in less than six months. In an effort to improve the absolute survival following amputation surgery, we have two adjunctive programs at the present time. These are randomized studies. The first involves immunotherapy in which transfer factor is obtained from long term survivors of osteogenic sarcoma. The second program involves chemotherapy and shows a great deal of promise. The combination chemotherapy program starts on day 15 and continues every four weeks with 12 treatments. The patient is given Vincristin 1.4 mg per meter square and 1500 mg of Methotrexate per meter square. This is injected intravenously over a four hour period. At the end of that time leukovorum 15 mg intravenous is given. The patient receives 12 mg of calcium leukovorum every four hours orally for three days. At 24 hours a dose of Adriamycin is given. Preliminary results with a similar adjunctive chemotherapy program. I think from the preliminary reports and our series we are increasing the disease free interval and statistical projection of these results suggests that we may obtain the same survival results with this program as we have experienced with the Ewing's sarcoma program and Wilms' tumor many years ago.

Dr. Morales, Miami, Fla.: If we see a tumor like this in soft tissue, we call it malignant fibrous histiocytoma. The inflammatory cells associated with this tumor may be considered to be a component of the tumor per se, since these are almost universally present in this type of soft tissue tumors.

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Eyre-Brook, A. L. & Price, C.H.G.: Fibrosarcoma of Bone. Review of Fifty Consecutive Cases from the Bristol Bone Tumor Registry. J. Bone & Jt. Surg. 5-1B: 20-37, 1969.

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8. Osteoblastic Osteosarcoma of the Distal Femur

Contributed by **Wm. Martel, M.D.** and **M. R. Abell, M.D.,** Ann Arbor, Michigan

The patient was a young man 17 years of age in June, 1973, when he gave a history of six weeks swelling in the left knee and of pain when running. On examination there was a 10 cm fixed tumefaction on the medial condylar area of the left femur. Laboratory test panel values were within normal limits. The alkaline phosphatase was elevated: 322 I.U. and the uric acid value was slightly above normal.

Dr. Hodes: The pertinent clinical data include the history of a painful swelling which proved to be a fixed tumor which had caused pain for six weeks in a seventeen-year-old male.

This is a rather classical bone forming malignant tumor. The calcified osteoid is the dominant feature although I believe that there is evidence of bone destruction or at least cortical destruction near the center of the tumor. The distal end of the femur is one of the favorite sites of most skeletal neoplasms, benign and malignant.

The rather solid nature of the tumor osteoid is associated with some periosteal proliferation. If we had a tangential view of the bony mass, one might more adequately be able to differentiate between an ordinary osteosarcoma and a parosteal sarcoma. The patient's age favors the former. The rather fluffy appearance of the tumor osteoid in the lateral view also favors the more common osteosarcoma rather than a perosteal osteosarcoma which tend to arise a little later in life and are much more dense.

Dr. Hodes Impression: Osteosarcoma

Radiologic Impressions Submitted:

Osteosarcoma	103
Parosteal sarcoma	29
Osteochondroma	03
Others	06

Dr. Hodes: As you see, someone else was worried about parosteal sarcoma. Osteochondroma? No way!

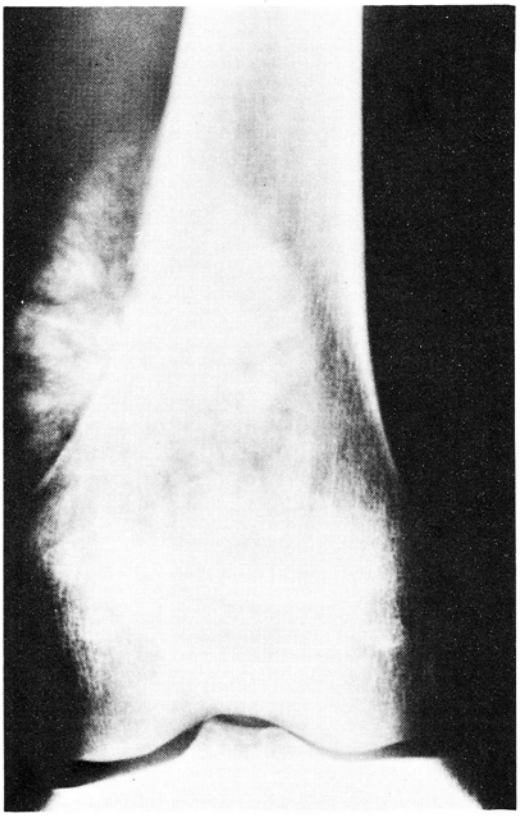


Fig. 1—Bone forming tumor of the femur with areas of destruction.

Dr. del Regato: Drs. Richard Mazzei, of Washington, D.C., S. Eisenberg, of Los Angeles, and H. A. Cherin, of Tampa, offered osteosarcoma. Dr. M. Levine, of Vancouver, Washington, and K. Latif, of Ann Arbor, suggested parosteal sarcoma.

The University of Missouri radiodiagnostic computer diagnosed osteosarcoma.

Operative Findings: On July 2nd, 1973, a high thigh amputation was done. The distal 30 cm length of the femur contained a tumor 9x6x5 cm which infiltrated the marrow and extended subperiosteally to the adjacent muscle.

Dr. Dahlin: This case is one of the most typical lesions in the group of 15. The individual cells are overtly malignant in that they are hyperchromatic and irregular in shape and contain abundant mitoses. Furthermore the microscopic section is dominated by the ability of these malignant cells to produce irregular trabeculae which are becoming mineralized. Here and there large vascular spaces are present and these probably represent a secondary invasion of blood into the malignant tumor. Radiographically with its osteosclerosis, cortical destruction, and bone production outside the cortex this tumor is typical osteosarcoma. Furthermore the epicenter of this tumor is in the metaphysis of the distal part of the femur, the most frequent location for osteosarcoma.

The only differential worth mentioning is telangiectatic osteosarcoma which diagnosis is suggested by the areas with large blood-filled spaces. I do not believe they are important.

Dr. Dahlin's Diagnosis: Osteoblastic Osteosarcoma, Grade IV

Histopathologic Diagnosis Submitted:

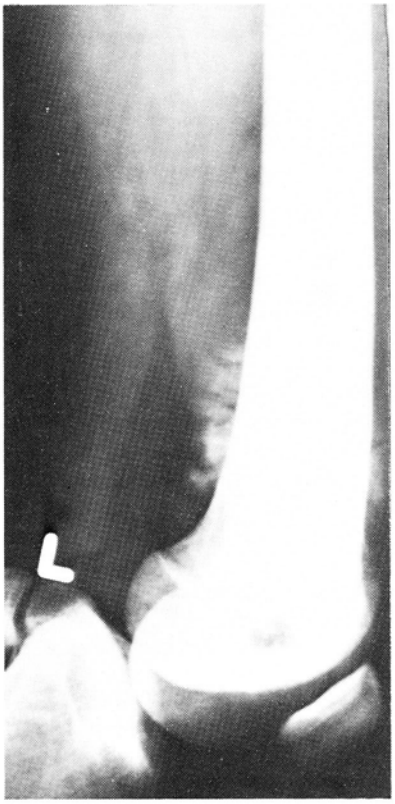
Osteosarcoma	98
Osteochondrosarcoma	01

Dr. del Regato: Overwhelmingly, our experts agreed on a diagnosis of osteosarcoma with only occasional suggestions that the origin might have been parosteal. One single correspondent, Dr. G. Vogt-Hoerner, of Paris, suggested osteo-chondrosarcoma.

Subsequent History: In May, 1974, ten months after amputation, the patient presented metastatic nodules in the base of the left lung. A left lower lobectomy was carried out. He was given 2,000 mgm of Cytoxan intravenously, 1.5 mgm of Vincristine per square meter of surface, 12.6 grams of Methotraxate and 12 mgm of folic acid every six hours. Subsequently, he also received Cyclophosphamide and Adriamycin and again Methotraxate and folic acid. Last seen in January, 1975, there was no evidence of recurrence or metastases.

Dr. Sim: This is a typical osteosarcoma that we see on a daily basis. The things that we mentioned are a careful pre-operative evaluation of the patient for metastatic disease, inter-surveillance testing of the patient, a careful open biopsy fol-

Fig. 2—Lateral view reveals periosteal proliferation.



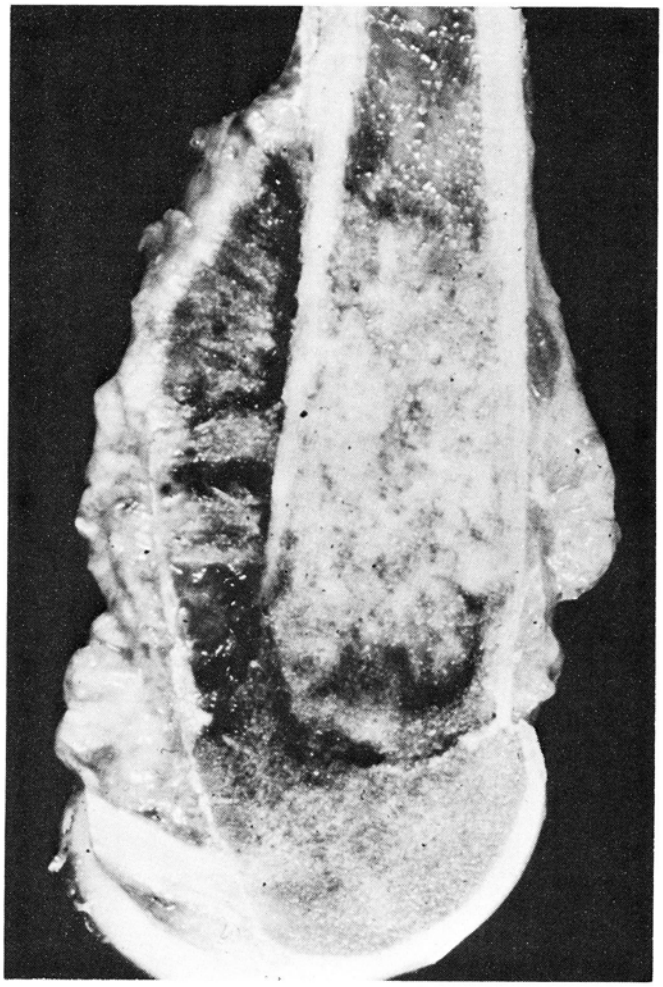


Fig. 3—Surgical specimen showing extension to adjacent muscle.

lowed by immediate amputation. The other thing of therapeutic significance is the rehabilitation of these patients. With modern techniques and immediate fitting of modern prosthesis, this young teenager can be standing at bedside the following morning and can be ambulated with prosthesis and crutches, within a week. This is of tremendous emotional significance for these

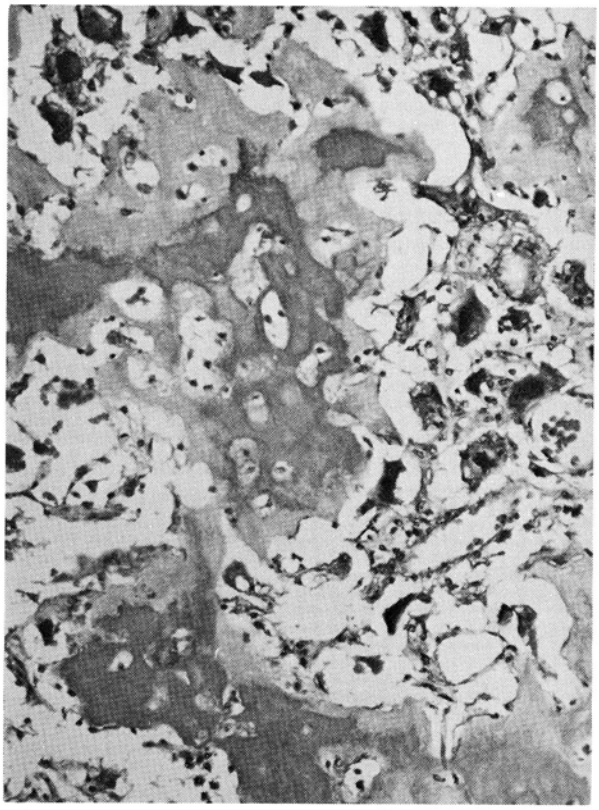


Fig. 4—Malignant cells of varied size and shape with frequent mitoses (x 250).

young people. Following the amputation and rehabilitation, they should be followed very closely: inter-surveillance testing, chest x-rays at monthly intervals and aggressive approach to pulmonary lesions, as well as the combined adjunctive immunotherapy or chemotherapy program.

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9. Ewing's Sarcoma of the Fibula

Contributed by **M. R. Abell, M.D.** and **Wm. Martel, M.D.**, Ann Arbor, Michigan

The patient was a girl, 13 years of age in October, 1972, when she complained of pain on the lateral aspect of the right knee. On examination there was a warm, erythematous mass on the lateral aspect of the right leg just below the knee. The laboratory test panel values were within normal limits. There was an elevation of the alkaline phosphatase, 223 I.U., and of the serum phosphorus, 5.7 mgm per cent.

Dr. Hodes: The clinical complaints in this thirteen-year-old girl were pain, local heat and mass just below the knee.

This is a predominantly destructive lesion which obviously has arisen within the medullary portion of the bone. It is infiltrating and destroying bone causing periosteal proliferation and some endosteal reaction. There is a lamellar periosteal reaction with a classical Codman cuff.

The mass extends well beyond the bone into the perifocal soft tissues where tumor osteoid is forming in a variety of patterns, some in classical onion skin manner, others in hair-on-end spicules and in others heterogeneously classified tumor osteoid. It is noteworthy that the cartilaginous plate of the epiphysis has not been invaded.

This is an obviously malignant tumor. Because we believe it has its origin in the medullary canal from which it has infiltrated in all directions, we believe it is a tumor of round cell type. And while the age of thirteen is a little beyond the classical first decade for Ewing's tumors involving tubular bones, the flat bones tending to be involved a little later, one must consider this a Ewing's tumor. The reticulum cell sarcomas or even metastatic neuroblastomas would produce the same lesion but statistically, accepting the postulate that this is a round cell tumor, the probabilities are we are dealing with a Ewing's tumor.

Dr. Hodes' Impression: Ewing's Sarcoma

Radiologic Impressions Submitted:

Ewing's sarcoma	113
Osteosarcoma	16
Osteomyelitis	11
Others	06

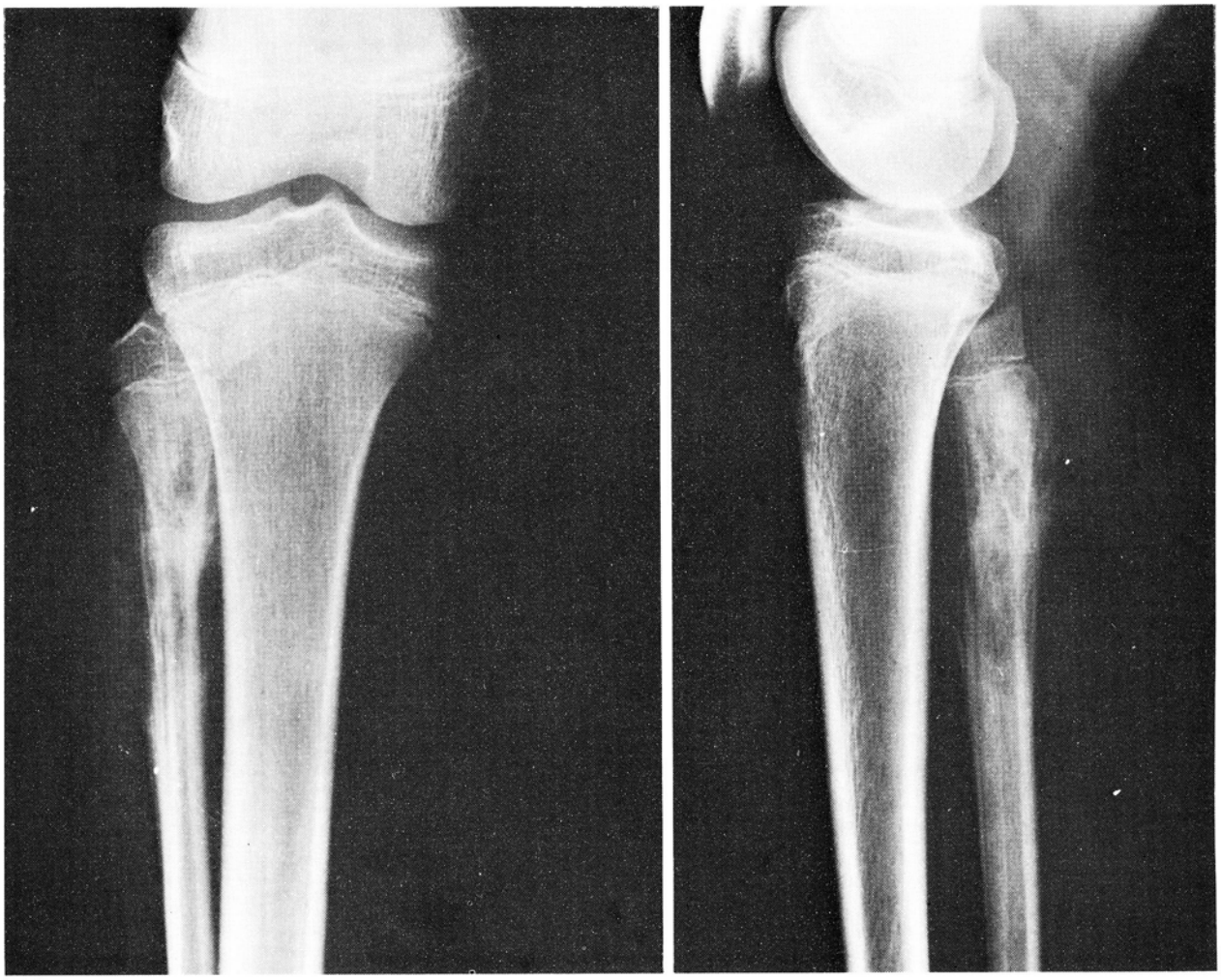
Dr. Hodes: I can't argue with a diagnosis of osteosarcoma; it is a likely diagnosis: the ratio of 16 to 113 is about the proportion you would expect. Osteomyelitis, for reasons I have given before, I could not go along with; but this is the condition with which Ewing's is commonly confused. The amount of bone that is involved is far too great.

Dr. del Regato: Most of our correspondents proposed Ewing's sarcoma with the usual second thoughts about neuroblastoma and possible lymphoblastic leukemia.

The University of Missouri radiodiagnostic computer diagnosed Ewing's sarcoma.

Operative Findings: On October 26, 1972, the right leg was amputated above the knee. The

Fig. 1—A & B. Destructive lesion of the medullary portion of the fibula causing periosteal proliferation.



surgical specimen contained a mass 10x6x4 cm involving bone and soft tissues. On cut section the tumor was soft, whitish and hemorrhagic.

Dr. Dahlin: This tumor of the upper portion of the shaft of the tibia in a 13 year old girl has produced roentgenographic destruction, obvious periosteal reaction, and soft tissue mass. In this regard it is characteristic of a primary bone tumor such as Ewing's sarcoma. Microscopically the tumor cells are distorted by large amounts of necrosis, but the islands in which they are viable indicate that they fit the small round cell malignant tumor group. In zones the nuclei are larger than in the classical Ewing's sarcoma but they still are most like those of Ewing's sarcoma. In areas the proliferating tumor cells are rather intimately admixed with proliferating osteoid trabeculae but these appear to be the result of reaction to the tumor rather than being part of the tumor. A reticulin stain of this tumor was not particularly helpful because of the marked degree of necrosis. In some areas, however, rather large clusters of cells without reticulin were present and this pattern is supportive evidence for Ewing's sarcoma. One would expect that a malignant lymphoma (reticulum cell sarcoma) of bone would contain argyrophilic fibers separating individual or just small clusters of cells. Also the cells of malignant lymphoma of bone should indicate their nature as they do in soft tissue tumors. It has been our experience, however, that in the borderline or problem cases this silver stain has not helped because it also has been equivocal. The PAS stain for glycogen in the material submitted to me shows only faintly positive glycogen droplets within the tumor cells. These tumor cells are not significantly different from those treated similarly but with diastase. Accordingly, it seems that the glycogen stain must be considered at best equivocal. In some tumors in which we have been forced to make the diagnosis of Ewing's sarcoma for histologic reasons, the glycogen stain has been negative. It is more comforting, however, when tumor cells of Ewing's do contain the PAS positive material that we can consider to be glycogen.

The differential diagnosis includes reticulum cell sarcoma which I have excluded for reasons mentioned above. Metastatic neuroblastoma could produce a pattern like this but it seems almost completely impossible in the fibula of a patient as old as 13 years.

Dr. Dahlin's Diagnosis: Ewing's Sarcoma

Histopathologic Diagnoses Submitted:

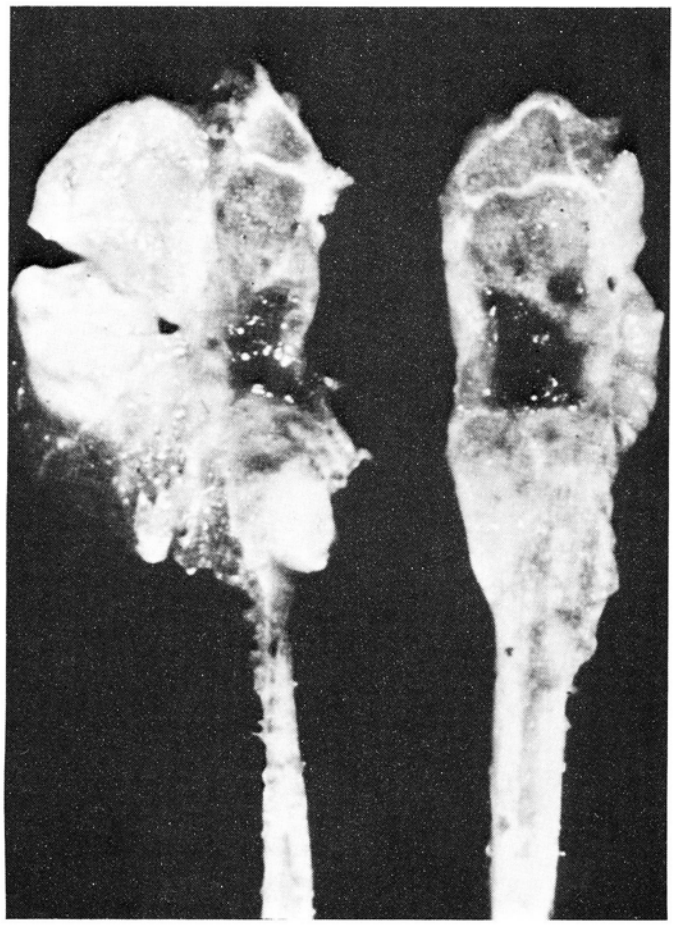
Ewing's sarcoma	69
Osteosarcoma	10
Reticulum-cell sarcoma	07
Others	16

Dr. Dahlin: I did not see anything to make me think that osteosarcoma was a reasonable diagnosis. I think the cells are too anaplastic to call them any variant of the malignant lymphoma group, which would include reticulum-cell sarcomas, but obviously, whenever we talk about small round-cell sarcomas, reticulum-cells sarcomas or malignant lymphoma, you expect about half the patients to become 5-year survivors. Another small round-cell lesion, that Dr. Jacobsen recently published, is polyhistioma. This may be a good term. I'm afraid that a lot of pathologists are not going to understand it well enough to accept it.

Dr. del Regato: Dr. Juan Rosai, of Minneapolis, considered Ewing's but, having seen malignant osteoid, offered osteosarcoma. Dr. S. A. Jacobson, of Vancouver, Washington, felt that the ossification and clear cells that he took to be lipoblasts, forced a diagnosis of polyhistioma.

Dr. W. K. Bullock, of Los Angeles, offered reticulum-cell sarcoma. Dr. L. H. Bernstein, of Washington, D.C., considered it an atypical Ewing's sarcoma because of the acidophilic cytoplasm. Drs. L. V. Ackerman of Stony Brook and H. A. Sissons, of London, both inquired as to the glycogen stain before committing themselves to a diagnosis of Ewing's sarcoma.

Fig. 2—Tumor involving the soft tissues.

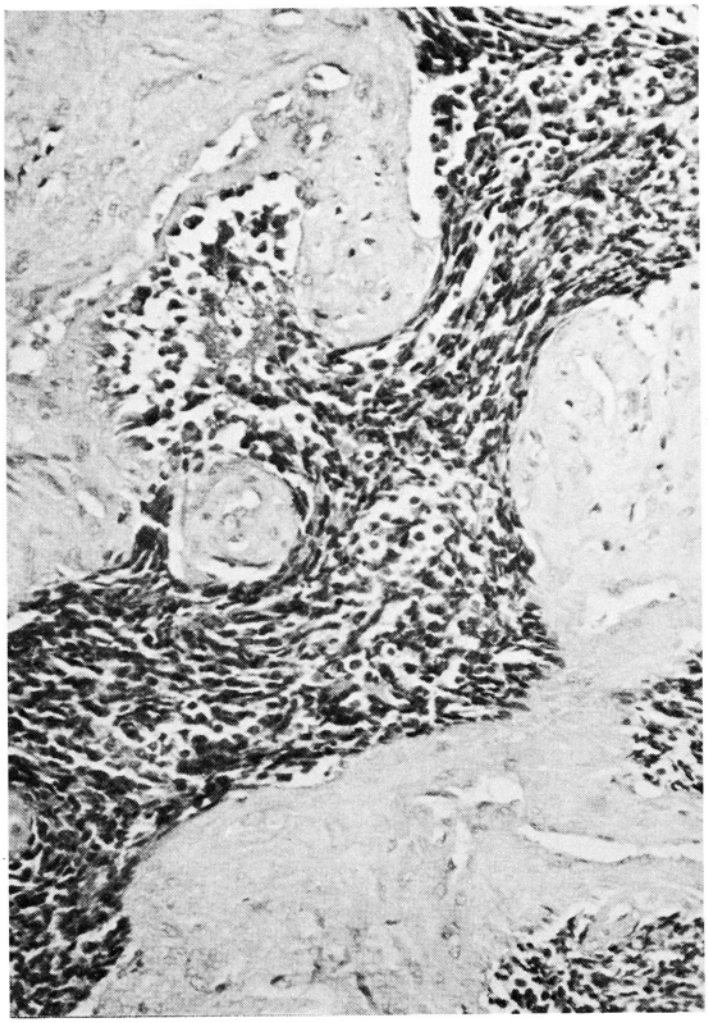


Dr. Lent C. Johnson, AFIP, Washington, D.C., wrote: There is reinforced cancellous bone in some, giving rise to areas of sclerosis. Between trabeculae the tumor is made of rather large undifferentiated round cells. The tumor is growing in dilated vascular channels in uninvolved areas of the bone and soft tissue. Areas of osteoid and chondroid production appear as non-neoplastic callus repair. Therefore, this is an undifferentiated round-cell tumor; it is customary to call all such, that cannot otherwise be named, as Ewing's tumor. The specific name implies a specific understanding of the tumor, which we do not have.

Subsequent History: Following surgery the patient was put on a regimen of chemotherapy. Metastases developed and the patient died November 27, 1974. No autopsy was done.

Dr. Sim: I think that from a clinical standpoint this case is quite typical of Ewing's sarcoma. The clinical presentation, the age, and the radiological manifestations are consistent with Ewing's. Whereas the former prognosis was perhaps a 15% five-year survival and a 10% ten-year survival, now with modern adjunctive therapy, the projected rates are much higher. In the January 1975 Journal of Bone and Joint Surgery, one of my colleagues reviewed the long-term survivors with Ewing's sarcoma and he found 37 out of 239 cases, and this brought up some very interesting points: The prognosis depended primarily on two factors; first, the location of the lesion in the central part of the skeleton had a poorer prognosis; this was in the neighborhood of 8%, whereas lesions in the extremities had 21% five-year survivors. The other striking and somewhat interesting finding was the treatment. In analyzing patients that had surgical treatment, which in most cases was amputation, there was a 44% five-year survival whereas in non-surgical treatment, the survival was 13%. I'm not recommending amputation treatment for Ewing's sarcoma, because modern treatment combining radiation therapy and polychemotherapy has known promising results. Since 1972 we have been following the protocol of the National Intergroup Ewing's Sarcoma Study; certainly, initial reports are very promising. In a case where the local lesion is not controlled with irradiation, or in some cases where there is some doubt in the diagnosis, amputation surgery may be indicated. Pomeroy recently reported on the projected survival figures with radiation therapy combined with long-term chemotherapy, over 18 months. Our study is randomizing patients with triple chemotherapy with or without prophylactic pulmonary irradiation. So far, the projected two-year survival rate is over 66% and the five-year survival is projected to 52%. These are indeed very promising and would indicate that we are in a new ball game.

Fig. 3—Round-cell malignant tumor distorted by large amounts of necrosis (x 250).



Dr. del Regato: The tumor described by Ewing as an endothelioma with characteristic rosettes, a fact that has been forgotten of late, is peculiar in view of the fact that the rosettes are also characteristic of neuroblastomas. The designation has long been a duffel-bag for tumors which are not in any way characteristic. When Oberling defined and segregated from the group, the reticulum-cell sarcoma as a primary lesion of bone, it removed most, if not all, of those eligible for cure. Some, as Rupert Willis, have always maintained that tumors diagnosed as Ewing's are often metastatic neuroblastomas or are placed in this category for lack of other choice. The question remains, as suggested by Lent Johnson's discussion, if such tumor exists and it is not possible to frame it in a diagnosable morphology, what are its other possible distinguishing features?

Dr. Szakacs, Tampa, Fla.: I would like to respond to that to some extent. The resolutions of the microscope is just so much. When other small-cell tumors are examined by the electron-microscope, they can be differentiated from Ewing's tumor cells.

Dr. del Regato: The point is that very often it is a diagnosis of exclusion. It is not so pinned down into a characteristic that can be readily recognized by the neophyte as well as the more experienced.

Dr. Cox, Milwaukee, Wisc.: Would Dr. Sim please be more specific about surgery in Ewing's sarcoma?

Dr. Sim: I think that we would recommend this patient for radiation therapy primarly in the neighborhood of 5 or 6 thousand rads. I've been impressed with improvements in recent years in radiation therapy. I've seen these patients have full irradiation, perhaps a little more in the area of the tumor and surrounding soft tissue. The skin looks extremely good, joint function is excellent. Following irradiation, the patient is enrolled in an 18-month course of chemotherapy. The role of surgery, you might consider, is as an additional means in indicated cases.

Dr. Howie, St. Petersburg, Fla.: Dr. Sim, what source of radiations would you use: conventional roentgentherapy, super-voltage cobalt?

Dr. Sim: Super-voltage perhaps.

Dr. del Regato: Insofar as these are usually young individuals and you want to have the maximum of benefit with a minimum of untoward effects, supervoltage radiotherapy is best utilized here. It is not a matter of the equipment, it is a matter of high quality penetration and the differential absorption between bone and soft tissues that is involved. As I pointed out earlier, when you use conventional radiotherapy, the differential absorption is heavy in bone as compared with soft tissue. When you use supervoltage radiotherapy or Cobalt 60 radiotherapy, the differential is minimal in the absorption between soft tissue and bone, so that would be the proper quality to use. The amount of radiations to be administered depends on various circumstances such as region, noble structures forcefully irradiated, size of the field, and above all, the planned total duration of treatments and number of fractions. That is a matter for the particular radiotherapist to judge, depending on those circumstances. To express a dose without qualification as to total time of delivery is as useless as to give the number of stitches in a surgical procedure; it means little.

Dr. Vuksanovic, Miami, Florida: In some cases of Ewing's sarcoma, a pathological fracture takes place; should there then be an operative intervention?

Dr. Sim: In patients with Ewing's sarcoma in whom a pathological fracture ensues, operative intervention must be seriously considered. The nature of the operative intervention would depend on the extent of the disease. If the investigation of the patient reveals that metastatic disease is present, then we would attempt to achieve secure internal fixation with methyl methacrylate combined with an internal fixation device. With the adjunctive use of methyl methacrylate with the internal fixation apparatus, the surgeon can now achieve his aim of secure fixation in the most extensive osseous destructive lesions. However, if a patient with Ewing's sarcoma that has been treated with radiation therapy has uncontrolled recurrent activity of the disease at the primary site associated with a pathologic fracture, then the surgeon must seriously consider amputation surgery. As we mentioned, radiation therapy to the primary lesion and adjunctive long-term chemotherapy is the treatment of choice in the management of Ewing's sarcoma. However, amputation may be beneficial in carefully selected patients, and several authors believe that amputation is the treatment of choice in distal lesions of Ewing's sarcoma.

Dr. Dahlin: As far as large-cell Ewing's are concerned, whenever the cells are larger than usual, I think we have to worry about two things especially: one of them is an osteosarcoma that we may not have sampled properly, but probably more important, is a malignant lymphoma. My rule has been that if the cells are so undifferentiated that we cannot comfortably say these are reticular cells or immature or more mature reticular cells or lymphocytes scattered through there, then we end up with calling it Ewing's—large cell: the indications are that they are about the same bad tumor. Lent Johnson says we don't know what Ewing's sarcoma is; I think he's right. It's a small round-cell undifferentiated tumor; there is some evidence that there are several tumors or diseases that can look like that, but in the present day knowledge, it is right to call it Ewing's sarcoma and perhaps somebody will shed light on this in the future.

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10. Osteoblastic Osteosarcoma of the Proximal Humerus

Contributed by **Eduardo Murphy, M.D.**, Mexico City, Mexico

The patient was a boy, 14 years of age in June, 1974, when he gave a history of trauma to his left shoulder six months previously. Pain had persisted and a physician had diagnosed bursitis. When the pain became worse, the examination revealed a deep swelling of the left arm near the scapular joint. The laboratory examinations were said to be non-contributory.

Dr. Hodes: The history of trauma and swelling in this fourteen year old lad is probably of no significance.

There is an extensive overgrowth of tumor osteoid which involves not only the metaphysis but obviously has crossed the epiphysis and involves the epiphyseal center of ossification. Extremely important is the tumor osteoid which extends beyond the main calcified osteoid. In addition there is a classical Codman's cuff which, though non-specific, attests to the violence with which this tumor is growing. Noteworthy is the fact that the Codman's cuff reveals very little reaction, a mark of a very rapidly growing neoplasm. And one can see tumor mass invading the medullary canal of the bone itself.

Of paramount importance is the calcified tumor osteoid beyond the confines of the bone and in the perifocal soft tissues. Hemorrhage alone would never account for this.

Dr. Hodes' Impression: Osteosarcoma

Radiologic Impressions Submitted:

Osteosarcoma	95
Parosteal sarcoma	29
Chondrosarcoma	08
Synovial sarcoma	05
Myositis ossificans	04
Others	08

Dr. Hodes: I hope that Dr. Dahlin will tell us a little about the so-called osteoblast. Chondrosarcoma? No way! This is calcified bone; this does not look like the calcified chondroid matrix. Synovial sarcoma, and of course, myositis ossificans? I can't understand either!

Dr. del Regato: Dr. M. Vallete, of Paris, hesitated between synovial chondrosarcoma and osteosarcoma. Dr. F. Convers, of Bogota, called it sclerosing osteosarcoma. Drs. C. Comstock, R. Kaufman, M. Graham, and G. Greenway of Ann Arbor, called it osteogenic sarcoma.

The University of Missouri radiodiagnostic computer diagnosed osteosarcoma.

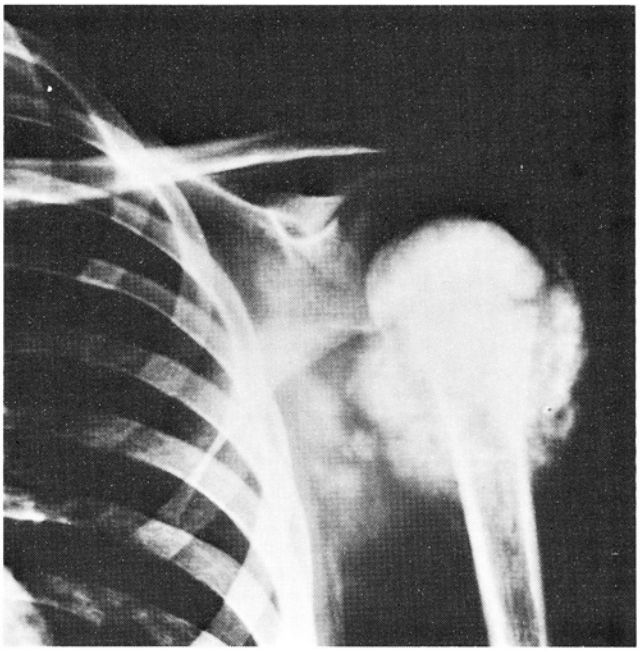
Operative Findings: On July 12th, 1974, an interscapulothoracic amputation was carried out. Cross examination of specimen was not permitted by relatives of the patient, who insisted on the burial of the removed arm.

Dr. Dahlin: This is an obviously bone-forming malignant tumor involving the upper metaphysis and epiphysis of the humerus and extending into adjacent soft tissues. Microscopically there is a predominance of irregular trabeculae of osteoid that is mineralizing. Their fine ramifications are very suggestive that the underlying tumor is malignant. Amongst the osteoid trabeculae are pleomorphic hyperchromatic nuclei that are larger than benign nuclei in size and contain fair numbers of mitotic figures.

No differential diagnosis is worthy of consideration.

My diagnostic conclusion is that this is osteoblastic osteosarcoma. It might be stated that a lesion like this in the upper end of the humerus in a 14 year old boy is characteristic in so far as age is concerned and the site is the third commonest for osteosarcoma in almost all large series.

Fig. 1—Extensive overgrowth of tumor osteoid on the humeral metaphysis.



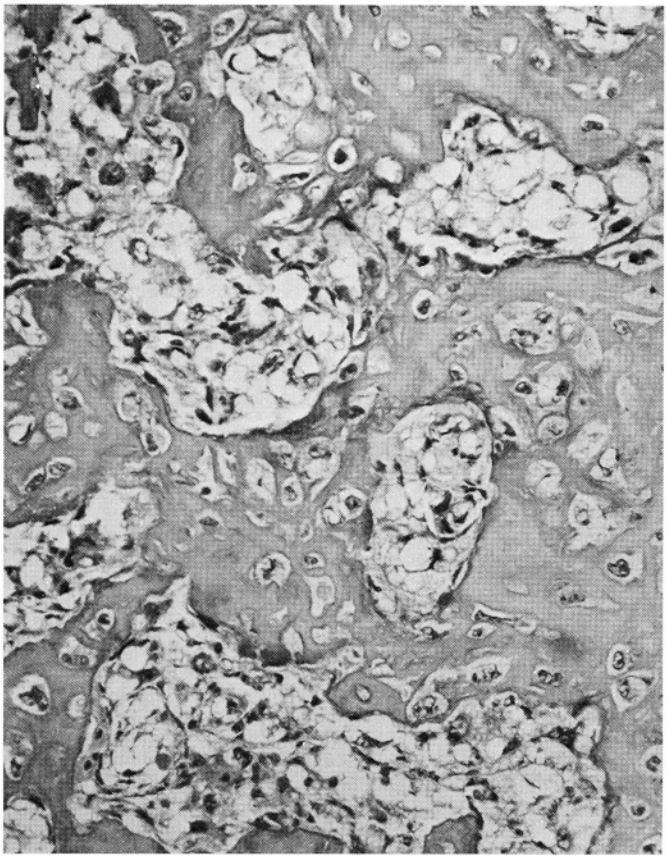
Dr. Dahlin's Diagnosis: Osteoblastic Osteosarcoma

Histopathologic Diagnosis Submitted:

Osteosarcoma (Juxtacortical 5)	64
Osteoblastoma	11
Osteochondroblastoma	08
Myositis ossificans	07
Others	03

Dr. Dahlin: This one is of so high-grade that I will just, categorically, not call it juxtacortical osteosarcoma. The question of osteoblastoma and whether it can, in rare instances, produce osteosarcoma or whether osteosarcoma can often resemble osteoblastoma is a big problem for everybody. I'm sure that it is far more common to see the problem of an osteosarcoma that is considered by some to be osteoblastomas erroneously than for a relationship of them to exist. I'll not comment on myositis ossificans either—it is not reasonable; however this is an important lesion. We teach our residents not to make diagnoses that are impossible, on the basis of what the surgeons tell us or what the roentgenograms show. I'd say that myositis ossificans is an impossible diagnosis in this case.

Fig. 2—Predominance of irregular tabeculae of mineralizing osteoid (x 250).



Dr. del Regato: Dr. W. K. Bullock, of Los Angeles also made a diagnosis of osteoblastic osteosarcoma. Drs. H. N. Hadders, of Groningen, Holland, H. A. Sissons, of London, and L. V. Ackerman, of Stony Brook, offered a qualified diagnosis of juxtacortical osteosarcoma. Dr. D. K. Davis, of Saint Petersburg, offered osteoblastoma. Dr. M. H. McGavran, of Hershey, Pennsylvania, considered it an aggressive osteoblastoma.

Dr. Lent C. Johnson, AFIP, Washington, D.C., wrote: Highly malignant tumor producing predominantly bone, but also small areas of cartilage. Because the bone is predominant, it is an osteosarcoma. I do not use the term osteogenic sarcoma. Tumors should be named for what they show, not for what they are presumed to come from.

Dr. Sim: This case points up the problem of delayed diagnosis with extension into the soft tissues. This would be a major therapeutic challenge at this time, in order to save the boy's life. In planning the operation, an arteriogram may be helpful in this case. I'm worried about involvement of the chest; in cases such as this, you would associate with the thoracic surgeon for an inter-scapulo-thoracic amputation with removal of part of the chest wall in the area of the direct extension. I think this could be something worth considering in this case.

Subsequent History: Shortly after operation, evidence of recurrence on the chest wall and of pulmonary metastases appeared. The child died on September 19th, 1974.

Dr. Murphy, Mexico: It would appear very advantageous to do bone scans.

Dr. del Regato: I am glad that the term "osteogenic" as applied to this tumor, is on the way out. The term intended, in fact, was not osteogenic but osteogenous, but we are better without it anyway. Osteosarcoma is perfectly satisfactory. For the sake of clearer semantics, we should now get rid of bronchogenic and say bronchogenous or simply say carcinoma of the bronchus.

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11. Mesenchymal Chondrosarcoma of the Pelvis

Contributed by **David C. Dahlin, M.D.**, Rochester, Minnesota

The patient was a 21-year-old man in December, 1971, when he gave a history of pain in the left hip and thigh, of three months duration. The physical examination failed to reveal gross abnormalities except for fullness of the left lower abdominal quadrant. The laboratory test values were within normal limits.

Dr. Hodes: The clinical history refers to pain in the left hip for three months in a twenty-four year old male.

There is an obviously destructive lesion involving the medial aspect of the acetabulum. Its perifocal transitional zone is totally indistinct and consonant with an aggressive process.

The large calcified mass which looks like calcified cartilage is well demarcated throughout its entirity with the exception of its inferior border. Here one notices rather classical calcific debris in crescentic or snowflake pattern associated with a perifocal soft tissue mass. It suggests that whereas at one time the main calcified mass may have been merely an osteochondroma, there is now evidence of malignant change manifested by the soft tissue mass, the fluffy somewhat crescentic calcified chondroid matrix and more especially the obvious osteolytic invasion of the region of the ischium and acetabulum.

Dr. Hodes' Impression: Chondrosarcoma

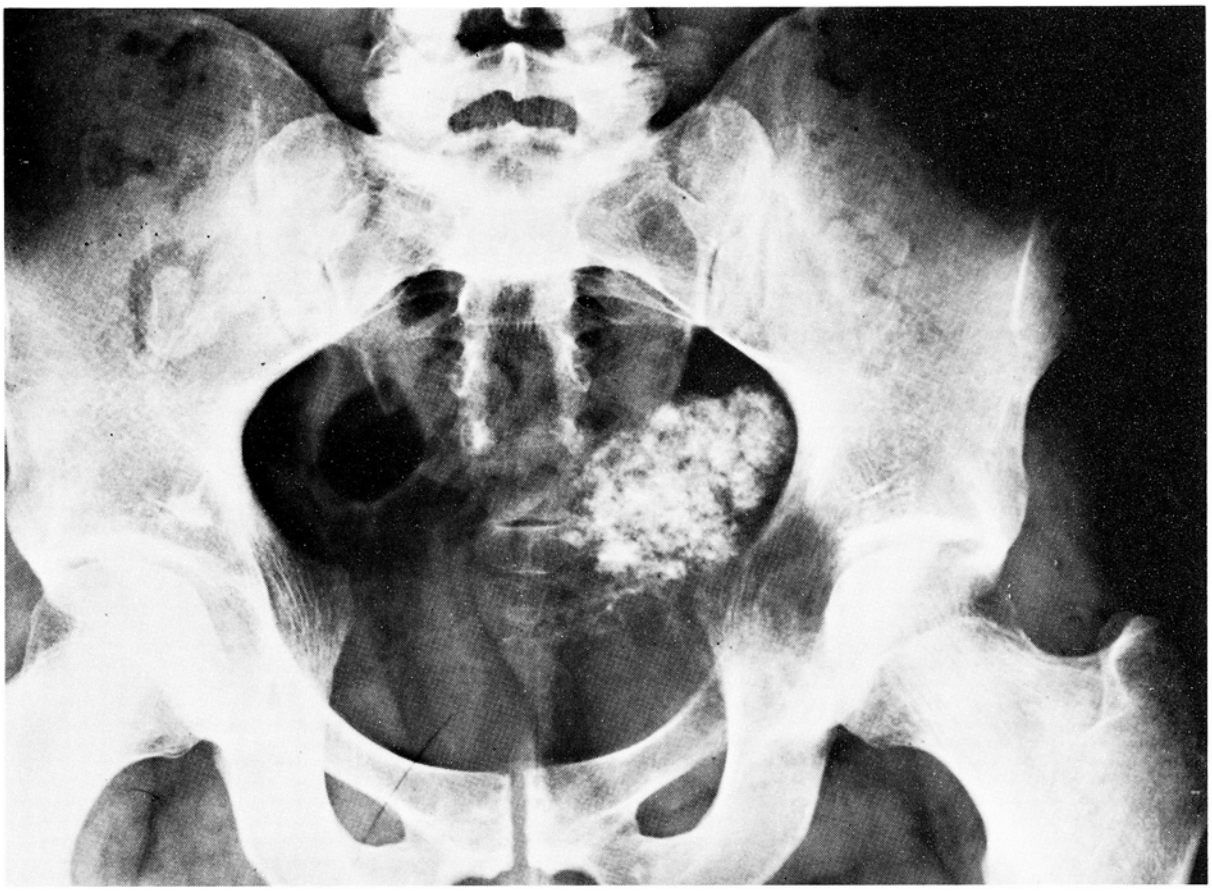
Radiologic Impression Submitted:

Chondrosarcoma	103
Osteochondroma	16
Osteosarcoma	07
Teratoma	05
Others	12

Dr. Hodes: For the reasons I have already given, we cannot consider this a benign condition. Let me give you a rule of thumb: Whenever I see a mid-line lesion and I don't know what it is, I'll call it dermoid or a teratoma. I'll be right more often than I'll be wrong!

Dr. del Regato: Dr. Luis O. Martinez, of Miami, offered an impression of osteochondroma. Dr. R. D. Bretz, of Long Beach, California, also suggested osteochondroma but could not rule out malignant transformation. Dr. R. C. Cavanaugh

Fig. 1—Calcified mass in snowflake pattern.



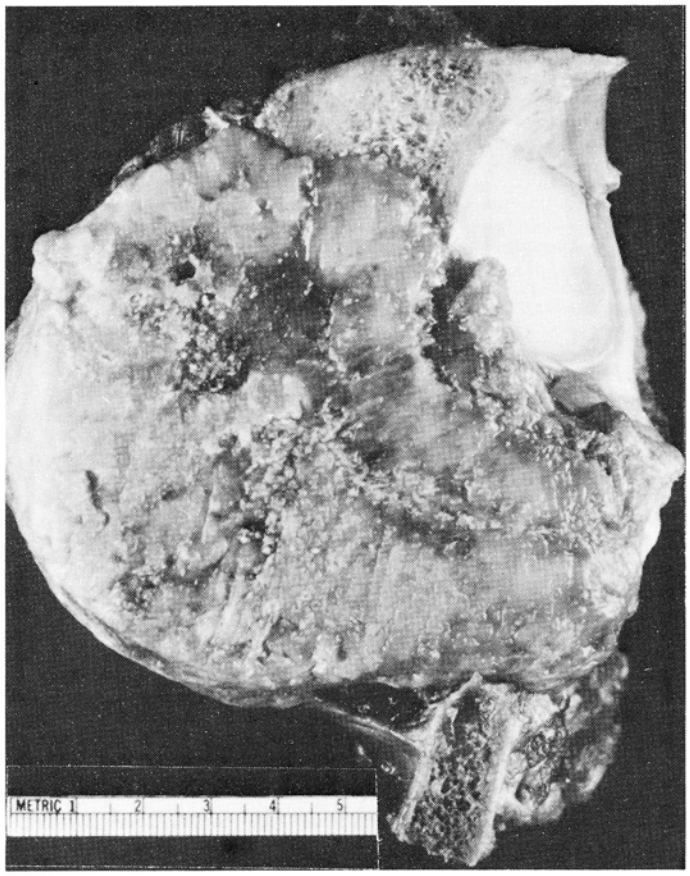


Fig. 2—Fragment of surgical specimen showing tumor.

of Boynton Beach, Fla. offered chondrosarcoma probably arising in an osteochondroma. Drs. R. Orr, of St. Petersburg, M. Soroudi, A. DeSmet and M. Wolfman, all of Ann Arbor, agreed to chondrosarcoma.

The University of Missouri radiodiagnostic computer diagnosed chondrosarcoma.

Operative Findings: In December, 1971, a hind-quarter amputation, including the acetabulum and portions of three pelvic bones, was carried out. The specimen contained a tumor 11x10x 10 cm which had eroded the fovea: it was completely removed.

Dr. Dahlin: This 21 year old man has a tumor that is lytic and destructive in the region of the acetabulum and has produced irregular and prominent calcification within the pelvis. Microscopically it is characterized by a bimorphic pattern. One of the elements in the section submitted is a component of small round cells that are undifferentiated. Some foci of necrosis are present and, in a few zones, the pattern of cells adjacent to thin-walled vessels suggest hemangiopericytoma. In other areas the small round cells are similar to those of Ewing's sarcoma. The second and very prominent element is cartilage which is only slightly malignant histologically. Matrix is abundant in the cartilaginous lobules. These in turn have areas of calcification due to the degeneration and zones in which the cartilaginous matrix is ossified. Accordingly, there are two factors that contribute to the mineralization seen by x-ray, calcification and actual ossification.

Really no differential diagnostic consideration is important when one recognized the bimorphic pattern with sheets of small round cells and lobules of cartilage. This pattern of mesenchymal chondrosarcoma has been recognized by the World Health Organization. I think the component of the matrix that is prominent in this tumor takes it out of the Ewing's sarcoma category. Tumors like this have been clinically about as malignant as osteosarcoma and the available evidence suggest they are radioresistent. Metastases are fairly common and they may appear well after 5 years from the time of first surgery.

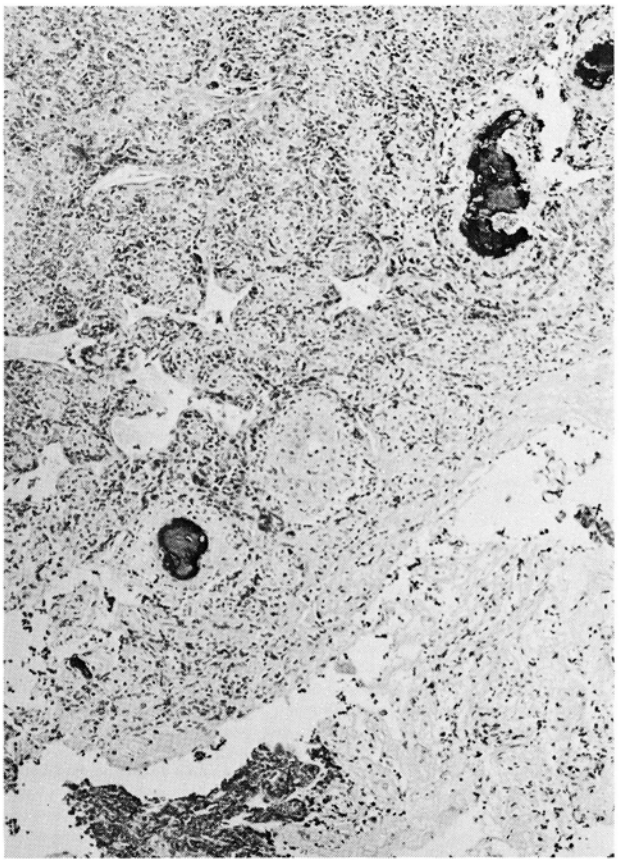
Dr. Dahlin's Diagnosis: Mesenchymal Chondrosarcoma

Histopathologic Diagnoses Submitted:

Chondrosarcoma	38
Mesenchymal chondrosarcoma	29
De-differentiated chondrosarcoma	06
Chondroblastoma	05
Others	15

Dr. Dahlin: When you say chondrosarcoma, you should qualify that term because this is a different chondrosarcoma than the average. The average has nothing that suggests Ewing's sar-

Fig. 3—Tumor formed by round cells with areas of calcification and of necrosis (x 80).



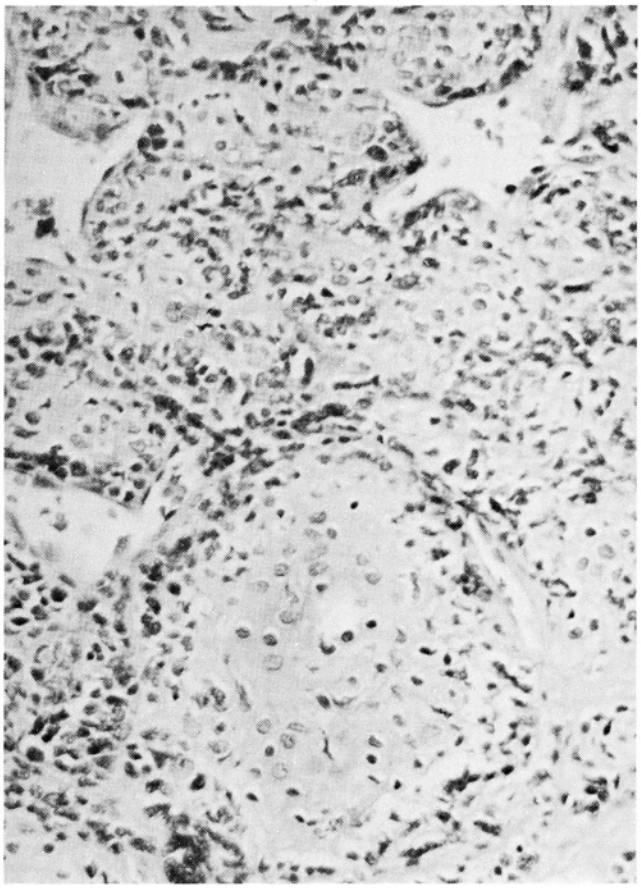


Fig. 4—Higher magnification shows a chondroid appearance (x 250).

coma in it. I don't think this even comes close to being de-differentiated because in that tumor, the more malignant element is composed of much larger nuclei than is present in the mesenchymal chondrosarcoma, larger nuclei as you expect to see in osteosarcoma or in fibrosarcoma. I did not see anything in this tumor to remind me of chondroblastoma.

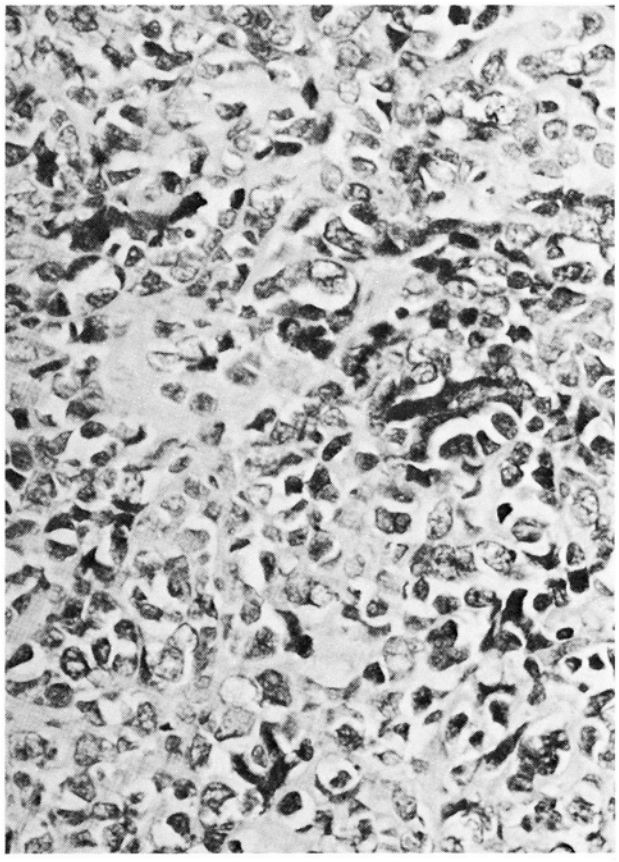
Dr. del Regato: Drs. C. Gouygou, E. Philippe and G. Conteso, of Paris, all agreed in a diagnosis of mesenchymal chondrosarcoma; Dr. Conteso indicated that the tumor had the appearance of a reticulum-cell sarcoma invading cartilage. Dr. J. Frerichs, of El Paso, also thought that this was an Ewings invading a chondroma. Dr. S. A. Jacobson, of Vancouver, Washington, looked upon it as malignant degeneration of a benign chondroblastoma. Dr. H. Spjut, of Houston, called it de-differentiated chondrosarcoma.

Dr. Lent C. Johnson, AFIP, Washington, D.C., wrote: Some areas of clear-cut cartilage are present with an abundance of sarcoma. Therefore, it is a chondrosarcoma. There are also sheets of pure round cells which could be taken for Ewing's, and thin chondroid strands that could be mistaken for a Codman tumor and a mesenchymal chondrosarcoma. Actually, it is a long-standing calcifying chondroma that has undergone malignant change and since the malignant component is producing cartilage, it is a chondrosarcoma . . . The term mesenchymal chondrosarcoma is being applied to completely undifferentiated chondrosarcomas, in which most of the tumor is made of sheets of cells, and also to very slow growing tumors that may run a twenty-year course without metastasizing. Obviously, the same term should not apply to both.

Subsequent History: The patient was examined in November, 1973, two years after operation, when he appeared free of recurrence or metastases. (Dr. Dahlin)

Dr. Sim: From the clinical standpoint, this case is a very typical chondrosarcoma. This is a common location for these cartilaginous tumors on the inner wall of the innominate bone. Lesions in this area may involve a long delay in diagnosis with symptoms before the lesion becomes apparent. These patients present with hip pain or a disk syndrome and we have seen many patients with myelograms in a search for the source of the pain. As in all primary malignant osseous lesions, it is important to survey the extent of the disease. In cases such as this, it is especially important to survey the local extent of the disease. An intravenous pyelogram would be helpful in showing the extent of the pelvic extension and perhaps an arteriogram would be helpful as well. To our best knowledge at the present time,

Fig. 5—Areas of the tumor had a resemblance to Ewing's tumor (x 400).



surgery is the mainstay of therapy for this radioresistant tumor and this would entail a hemipelvectomy. However, in planning the surgery there are several important points to be made about the biopsy. An open biopsy is preferred. It must be carefully placed so as to prevent tumor implantation. As you know, these cartilage tumors are notorious for wound implantation and recurrence. Many times we see patients with improperly placed biopsy incisions. This makes planning the definitive surgery with complete excision very difficult. This is particularly true if the biopsy has been carried out transperitoneally. In planning the surgery, it is important to determine the extent of the lesion posteriorly. It is always discouraging when one cuts across the posterior ilium and finds that there are still tumor cells present. This case would necessitate a complete disarticulation at the sacroiliac joint. In this case it is very pleasing to see the patient still alive after two years. However, in our experience with mesenchymal chondrosarcomas, there is a great variability in the clinical course and metastasis may occur well after five years from the time of initial surgery. Therefore, the long followup is necessary.

Dr. Sim: Dr. Dahlin, if you were grading the chondrosarcoma elements, what grade would it be?

Dr. Dahlin: This case is borderline for malignancy; tumors that we recognize as mesenchymal chondrosarcoma are generally low-grade or almost benign.

Dr. Azar: I would like to submit that the term mesenchymal chondrosarcoma is a most unfortunate one. I have always been told, and I teach, that all genuine sarcomas, with the great exceptions of malignant schwannoma, producing mesenchymal elements are mesenchymal. Dr. Stout used to call them malignant mesenchymomas, when you have two unreconcilable elements in addition to fibrosarcoma. He was very keen on excluding the fibrous element and he also tried to see repeatedly, the hemangiopericytoma elements which fortunately can be seen in a variety of other tumors. If we exclude these two, you end up with very little certain round cells which, if stained properly, can be due to nothing but chondroblasts.

Dr. Dahlin: I can sympathize with Dr. Azar in not liking the term, but I don't think he has provided us with a better one.

Dr. Azar: Poorly differentiated chondrosarcoma, type Dahlin-Lichtenstein.

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12. Giant-Cell Tumor of the Distal Femur

Contributed by **Carlos F. Arazoza, M.D.,** El Paso, Texas

The patient was a 22-year-old woman in February, 1974, when she complained of persistent pain in the right knee. Pain was elicited upon palpation of the lateral aspect of the right thigh near the knee. The bone scan indicated the presence of a neoplastic lesion. The alkaline phospatase was 15 K.A.U.; the serum calcium was 10.4 mgm per cent; the acid phosphatase was elevated: 1.75 sigma units.

Dr. Hodes: Pain in the right knee in this twenty-two year old young lady was associated with a positive bone scan. In our experience the bone scan merely points up the presence of an abnormality.

Here we have a rather classical eccentrically placed para-articular metaphyseal lesion which approaches the joint. It is seen to better advantage in the lateral projection where its distal margin is sharply demarcated with a well developed zone of reactive bone. In the lateral projection the transition between the osteolytic lesion and the normal bone is rather an abrupt transition rather than the permeative transition one sees with a neoplasm. The new trabeculae that traverse the lesion probably represent the remnants of residual cortex eroded by the osteolytic process. The latter has caused definite changes in the medial aspect of the femoral condyle, the cortex of which is thin but not violated. In a patient twenty-two years of age, these roentgenographic findings are consonant with the divanosis of a giant cell tumor. In this case I would be inclined to call it a benign giant cell tumor because of its rather classical appearance.

Dr. Hodes' Impression: Giant-Cell Tumor

Radiologic Impressions Submitted:

Giant-cell tumor	99
Chondroblastoma	17
Fibro-, osteo-sarcoma	09
Aneurysmal cyst	08
Others	13

Dr. Hodes: I don't make the diagnosis of chondroblastoma very often. I usually like to see more bone reaction than I see in this individual. There is nothing whatsoever about this that made

me think of a malignant lesion; as far as the aneurysmal bone cyst, we discussed that previously.

Dr. del Regato: Drs. R. L. Washburn and E. Chlosta of Ann Arbor, and Dr. M. C. Baird of Long Beach, California, offered an impression of giant-cell tumor. Dr. L. N. Schulz, of Cincinnati, thought it to be malignant. Dr. F. Convers of Bogota, called it benign. Dr. R. Mendoza-Rojas, of Mexico City, preferred aneurysmatic cyst. Drs. G. Lodwick and C. Farrell of Columbia, Missouri, favored giant-cell tumor.

The University of Missouri radiodiagnostic computer diagnosed giant-cell tumor.

Operative Findings: On April 1st, 1974, the lesion was thoroughly curetted out, the walls were cauterized with carbolic acid and cancellous bone was put in the cavity. About 250 gm of curettings were obtained and examined.

Dr. Dahlin: This tumor occurred in the distal end of the femur in a 22 year old woman; thus giant cell tumor becomes a distinct possibility. Microscopically the significant component again is the prominent mass of mononuclear cells which are reasonably regular in size and shape although mitotic figures are fairly common. The mononuclear cells in diagnostic zones are producing nothing except multinucleated forms, the nuclei of which are like those of the mononuclear cells. Areas in which the mononuclear cells are associated with considerable fibrogenesis and even osteoid production are present here and there but again these are not characteristic of the lesion itself. Perhaps more important in this case is the liberal component of blood-filled areas which introduce the possibility one might be dealing with an aneurysmal bone cyst. In this regard it is worth remembering that a fair number of giant cell tumors especially after a fracture or prior treatment show prominent blood-containing areas. In such cases the diagnosis of giant cell tumor can be established by paying attention to the non-bloody portions of the tumor.

The differential diagnosis again would include sarcoma but the cells of this tumor are not overtly malignant. In addition aneurysmal bone cyst should be considered but should be discarded because of the characteristics of the non-bloody zone.

Dr. Dahlin's Diagnosis: Giant-Cell Tumor

Histopathologic Diagnoses Submitted:

Giant-cell tumor (plain)	38
Giant-cell tumor (malignant)	13
Giant-cell tumor (benign)	09
Aneurysmal cyst	08
Hyperparathydroidism	07
Others	08

Dr. Dahlin: Most of the pathologists who saw this regarded it as giant-cell tumor. I did not

Fig. 1—Eccentrically located para-articular lytic lesion of the distal femur.

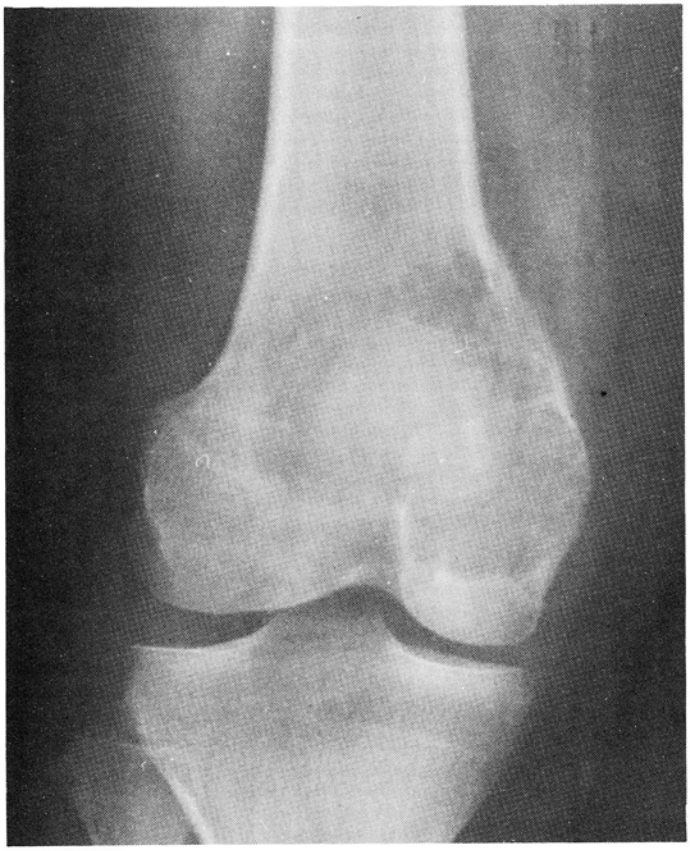
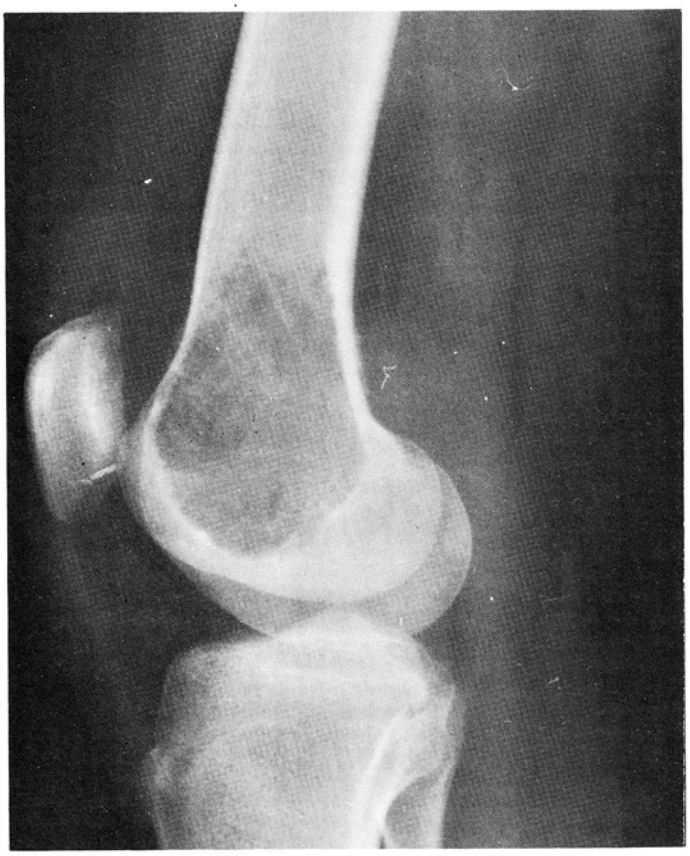


Fig. 2—Rather abrupt limits of the osteolytic process.

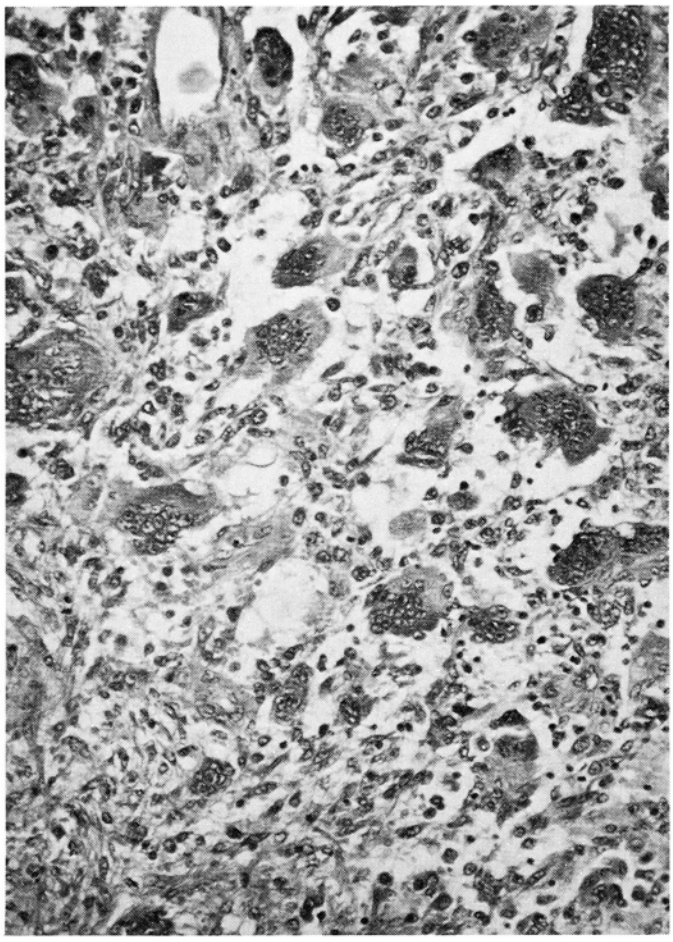


think that the stroma cells were bad enough to be worrisome enough to call it a malignant giant-cell tumor. The blood spaces did, in fact, look somewhat like aneurysmal bone cyst. Hyperparathyroidism should not give such a good radiographic image of giant-cell tumor; I would assume that you could do serum calcium studies to look for evidence of that disease.

Dr. del Regato: A diagnosis of non-committal giant-cell tumor was offered by Drs. G. Vogt-Hoerner, of Paris, and by Fritz Schajowich, of Buenos Aires; a connotation of benign was added by Drs. C. P. Schwinn, of Los Angeles and L. H. Bernstein, of Washington, D. C. Dr. H. N. Hadders, of Holland heeded the pleomorphism and the number of mitoses, concluding to malignant giant-cell tumor, and advising amputation. Drs. B. Castleman, of Boston, S. A. Jacobson, of Vancouver, Washington, and D. K. Davis of Tampa, were concerned with the serum calcium and with ruling out hyperparathyroidism.

Dr. Lent C. Johnson, AFIP, Washington, D.C., wrote: The histology is typical of a giant-cell tumor. There is nothing in the x-ray or histology to raise a question about malignancy. A bit of osteoid in a malignant giant-cell tumor does not change the name to osteosarcoma. A giant-cell tumor is proven malignant by pulmonary metastases that look the same as the bone tumor.

Fig. 3—Mass of mononuclear cells producing multinucleated forms.



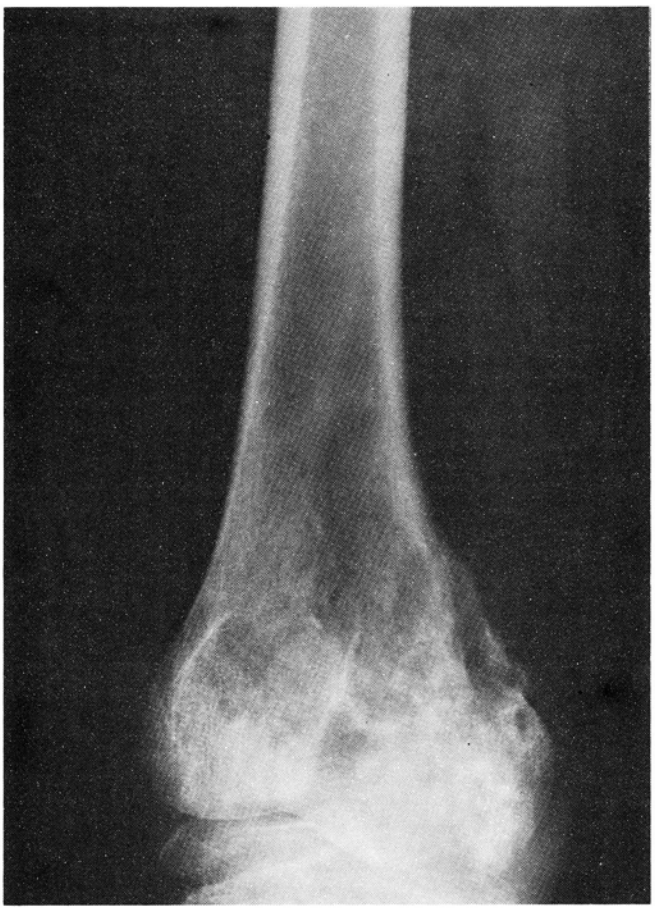


Fig. 4—Follow-up roentgenogram one year after treatment.

Subsequent History: In November, 1974, the patient was examined radiographically: there was no evidence of recurrence. In March, 1975, the patient is in good health and is even able to run.

Dr. Sim: This case presents the usual therapeutic challenge that we see in giant cell tumors in this area. Depending on the extensiveness of the lesion with soft tissue involvement, complete resection of the distal femur may be necessary sacrificing the integrity of the knee joint. The lesion is extensive. The lateral cortex has been destroyed and the destruction extends to the anterior and posterior cortex. However, I think that in a lesion of this nature we would be able to control the disease and yet preserve the joint. A complete excision of the lateral cortex excising the anterior and posterior cortex and completely exteriorizing the tumor cavity yet preserving the articular surface will allow us to completely excise the tumor with a curette. If we are going to control the disease, complete excision of all tumor is required. However, in this case, I think the joint can be preserved. The integrity of the

distal femur can then be restored with iliac bone grafts.

Dr. Font, Silver Spring, Md.: I have a question for Dr. Dahlin. When we are confronted with a benign form of a giant-cell tumor and the question comes of the differential diagnosis with aneurysmal bone cyst, how much do you rely on the finding of osteoid lining these vascular spaces? It has been shown in different textbooks that the presence of osteoid along the vascular channels is highly characteristic or perhaps pathognomonic for an aneurysmal bone cyst. How do you feel about that?

Dr. Dahlin: A problem of differential diagnosis between aneurysmal bone cyst and giant-cell tumor is rare. Giant-cell tumors are mostly clear-cut but there are rare cases where a problem does exist. I don't remember having seen long strands of fibroid bone as it is characteristically seen in aneurysmal bone cyst, in blood spaces in the giant-cell tumor. I am sure it could occur but it would make me lean towards aneurysmal bone cyst. We should keep in mind that it is really unusual to have this problem of differential diagnosis.

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13. Low-Grade Hemangiopericytoma of the Sacrum

Contributed by **J. R. Gutierrez, M.D., H. Azar, M.D.** and **J. Bolivar, M.D.**
Tampa, Florida

The patient was a 45-year-old man in April, 1973, when he gave a history of hematuria and nycturia of six months' duration; he had also developed dyspnea of effort. On examination, a large, firm, non-tender mass was felt on the left side of the rectum. CBC and other laboratory tests were within normal limits.

Dr. Hodes: Hematuria, nycturia plus the presence of a firm non-tender mass in the rectum are the hallmarks of this forty-five year old man's clinical history.

The osteolytic lesion in the pelvis is asymmetrical. It has a totally irregular transitional peripheral zone consonant with an aggressive tumor. It is not a very aggressive tumor as there tending to envelope the lesion, which are manifested, particularly along the superior and lateral margin.

In all sacral lesions one thinks of the presacral dermoids, chordomas and metastatic disease.

The angiogram excludes a simple presacral dermoid. The vascularity is consonant with a malignant tumor.

Extremely important is the asymmetrical site of origin of the involvement. Chordomas classically are centrally placed though occasionally they may be eccentric. The vast majority, however, are centrally placed. Also, they extend as a mass into the presacral region and may be felt rectally. We are told nothing as to the nature of a primary lesion elsewhere which may have metastasized to the pelvis.

At the age of forty-five one must always consider plasmacytoma.

Because this is not a centrally placed lesion and because we do not have a true lateral which would define for us the limits of the tumor, I am inclined to exclude chordoma.

Dr. Hodes' Impression: Metastatic Carcinoma

Radiologic Impressions Submitted:

Chordoma	53
Metastatic tumor	36
Fibro (neuro, chondro) sarcoma	23
Giant-cell tumor	11
Various, benign	19
Various, malignant	17

Dr. Hodes: I'm not surprised that a number of participants called this a chordoma; I think the fact that it was not in the mid-line militated against it. The vascularity which was present made me think of metastatic disease. Giant-cell tumor; I originally thought of until I saw the angiogram.

Dr. del Regato: The location of the lesion drew most radiologists to the logical conclusion of chordoma; the bone destruction made others think of the possibility of a metastatic tumor. Drs. G. Lodwick and C. Farrell offered chordoma.

The University of Missouri radiodiagnostic computer diagnosed soft tissue sarcoma.

Operative Findings: On May 15th, 1973 an exploration of the pelvis revealed an apparently well-encapsulated multilobated mass attached to the sacrum. A wide excision was carried out. The specimen measured 12x9 8.5 cm. On cut section it appeared formed by bundles of gray-white

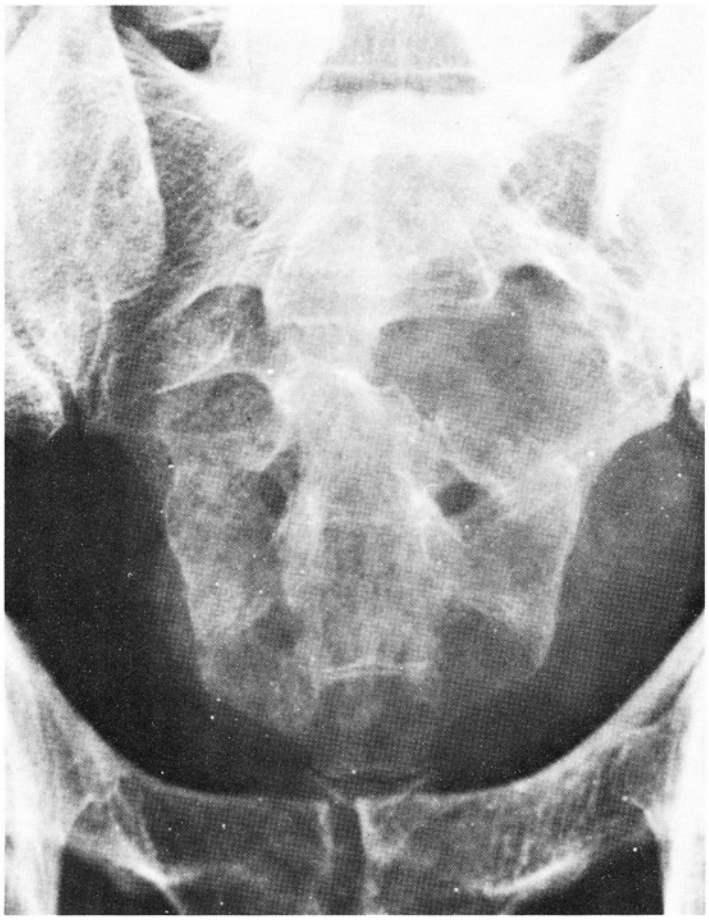


Fig. 1—Eccentric osteolytic lesion of the left side of the sacrum.

tissue forming lobules, some of which were 5 cm in diameter.

Dr. Dahlin: Case 13 represents an unusual bone tumor and it is possible, or probable, that the tumor is of soft tissue derivation and has secondarily invaded the sacrum where it has produced a malignant appearance by x-ray. The component cells contain nuclei that are somewhat spindle-shaped. They are rather closely compacted but separated by stainable collagen. Mitotic figures are present but not abundant. The hallmark of this tumor appears to be that the proliferating cells are most prominent outside small vascular channels and have bulged into them to produce a tufting appearance. Reticulin stains demonstrate that the proliferation is outside the capillary membrane and this appearance is correct for hemangiopericytoma. Our experience with tumors like this is that they have a fairly prominent capacity for local recurrence but metastases are distinctly unusual. Nevertheless metastases are possible and may be rather long delayed in their appearance.

The differential diagnosis would include hemangioma or hemangioendothelioma but the reticulin stain demonstrates that the cells are pericytes. Fibrosarcoma of bone does not demonstrate a vascular pattern such as this.

Dr. Dahlin's Diagnosis: Low-Grade Hemangiopericytoma

Histopathologic Diagnoses Submitted:	
Hemangiopericytoma	59
Histiocytoma	10
Fibro (angio, xantho) sarcoma	17
Hemangiosarcoma	11
Others	09

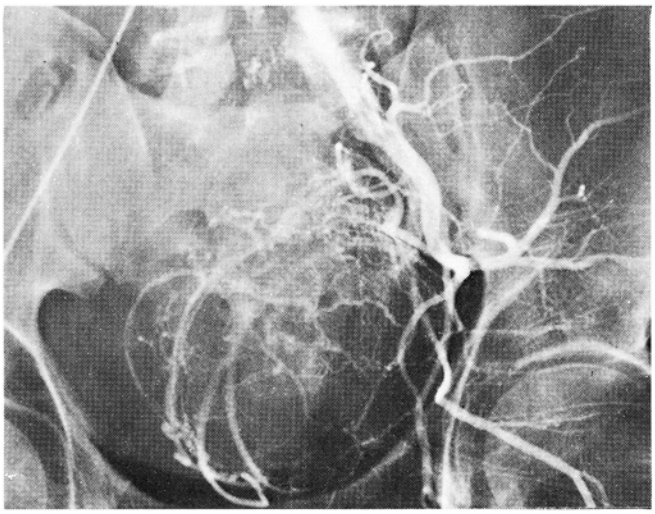
Dr. Dahlin: I think this lesion is definitively hemangiopericytomatous and, therefore, fibrosarcoma would not be correct. Neither would histiocytoma, by the same token. The fact that some participants regarded this as hemangiosarcoma indicates again how these tumors almost curve one into the other, as far as histology is concerned.

Dr. del Regato: Drs. C. F. Farinacci, of San Antonio, A. L. Vargas, of El Paso, N. Heldt and X. Walter, of Paris, also diagnosed hemangiopericytoma. Dr. A. D. Johnston, of New York City, offered malignant fibrous histiocytoma. Dr. J. M. Vetter, of Paris, suggested "glomangioma." Dr. R. Blache, of Paris and Dr. L. Clowry of Tampa preferred anaplastic hemangiosarcoma. Dr. H. Azar, of Tampa, whose case this was made a diagnosis of benign fibrous tumor with features of hemangiopericytoma.

In June, 1973, Dr. F. M. Enzinger, of the Armed Forces Institute of Pathology, was consulted on this case (Accession Number 1446928); he made a diagnosis of hemangiopericytoma and commented that fibrosis and myxoid changes have been observed in such cases. He also stated that the number of mitotic figures and the presence or absence of areas of hemorrhage and necrosis are most important in determining the clinical course. On this basis, he predicted a **benign course** for this case. Dr. R. Lattes, of New York, who was also consulted originally, suggested a malignant transformation in a pre-existing neurofibroma.

In 1975, Dr. Lent C. Johnson, AFIP, Washington, D.C., wrote on this Cancer Seminar slide:

Fig. 2—Angiogram showing marked vascularity.



Dr. Enzinger and I agree that this is a hemangiopericytoma. There is enough variation in size, shape and staining intensity so that it should probably be called a **malignant** hemangiopericytoma.

Subsequent History: Since operation, the patient has done rather well. In August, 1974, he had some constipation and blood in the stools. Barium enema and intravenous pyelogram revealed no abnormalities. On March 3rd, 1975, he acknowledged no discomfort or pain, is working part-time.

Dr. Sim: All sacral tumors present great diagnostic and therapeutic challenges, both to orthopedic surgeons and neurosurgeons, and in cases like this because of the pelvic extension, to gynecological and general surgeons. The choice of treatment depends on the location and also the extent of the sacral tumor. Complete surgical operative evaluation (proctoscopy, IVP, barium enema, angiogram) will help determine the extent of the bone destruction. Perhaps tomography could show the extent of osseous involvement to greater advantage before considering resection. Generally, one would advise resection of the lesion. We know that an uncontrolled malignant lesion in this area would only lead to further progression and invasion of the nerves, loss of bowel and bladder function, and tumor ulceration; and an effort should be made at radical resection of these lesions. Two considerations are present. First what neurological deficit would we be willing to accept with the resection and the second consideration is the possible creation of pelvic instability. In this location, one would anticipate causing a deficit of S2 and S3, but with preservation of the nerves on the opposite side, bowel and bladder function should be preserved. Beyond this concern, I think that every effort should be made at complete surgical removal of the lesion.

Dr. Azar: I think that this is probably a benign fibrous tumor with features of hemangiopericytoma. The bulk of this tumor did not present the features that were shown by Dr. Dahlin. Most of this was plain fibrous tissue. Dr. Bolivar sent us repeated pieces, from frozen section, and when the whole tumor came in, we saw a large mass and most of the latter was actually fibrous tissue. The concept of hemangiopericytoma is undergoing very rapid change. It was apparent right in the laboratory of Dr. Stout when we began thinking in terms of hemangiopericytoma as a histologic feature that does not stick with one particular histogenetic type. We see it in neurofibroma; we see it with vascularized myeloma, sometimes in tumor of the pancreas and in tu-

Fig. 3—Gross appearance of surgical specimen.

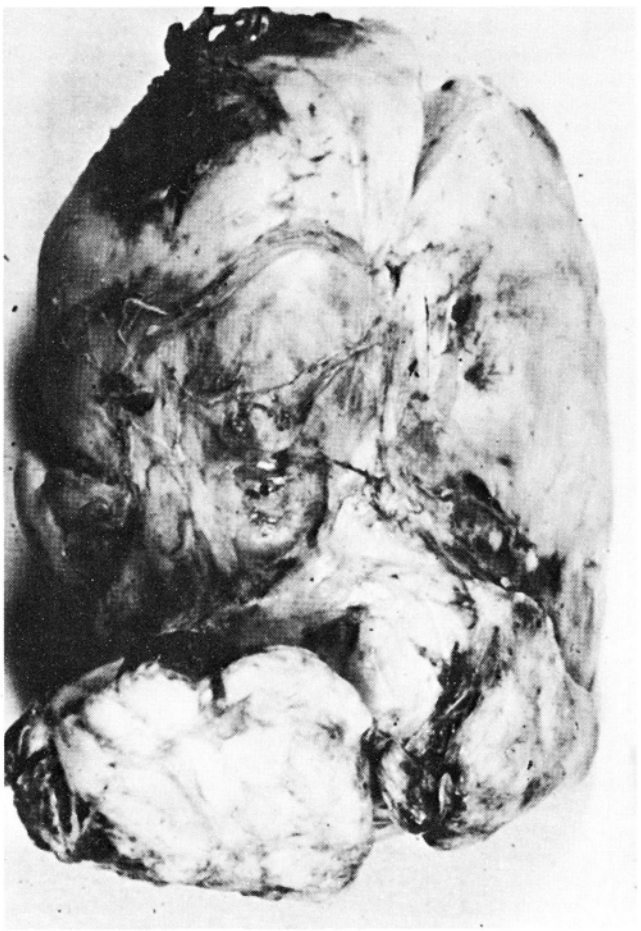
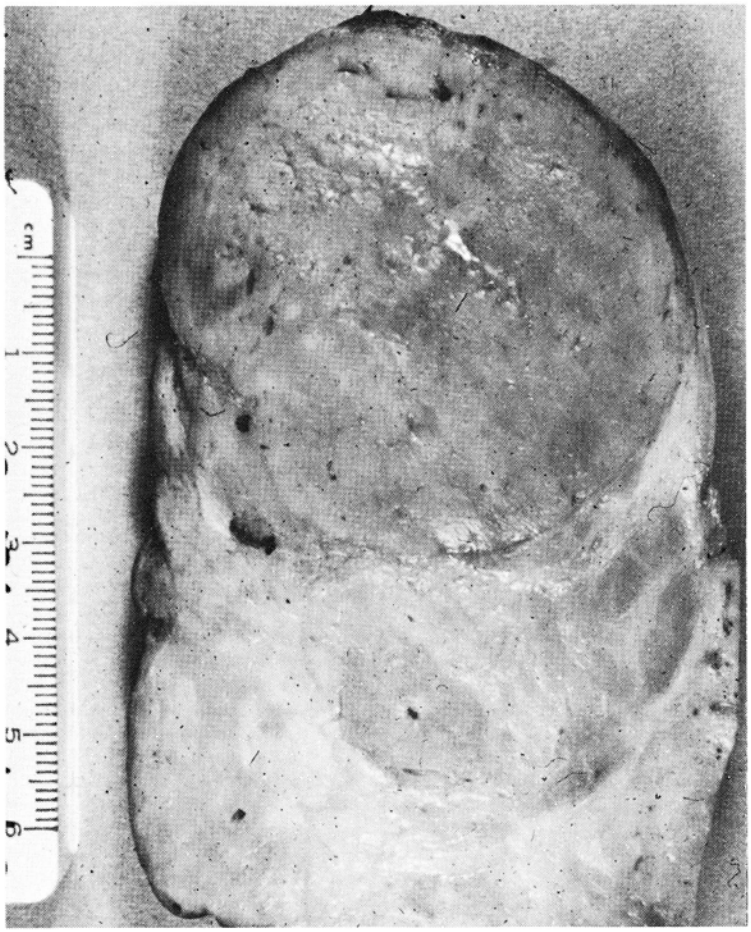


Fig. 4—Cut section of tumor.



mors of the ovary. I am sure that we are going to change our ideas about hemangiopericytoma and not accept it as a specific histologic diagnosis.

Dr. Font: In a collection of tumors, of 2500 cases, we have been following, there was a group of 300 or 400 tumors that we classified hemangiosarcomas. Recently, one of our fellows, Dr. Jacobi, did electromicrophotography in well-fixed material of one of these tumors; one can see that the pericyte is a distant cell in that the cells are practically embedded or surrounded in the basal membrane. There is a scarcity of organells; there are some scattered microfilaments and their focal density is along the primal limb, so by electromicrography, the pericyte can be very readily distinguished from endothelial cells, from fibroblasts, from histiocytes.

Dr. Perez-Mesa: I was present when Dr. Ludwick was making his personal diagnoses and then feeding the data to the computer in these Cancer Seminar cases. I feel that in the first cases the computer did pretty badly, particularly on two or three different occasions, whereas in the latter cases the computer did better and made even the diagnoses of soft tissue tumor. This was pretty good. I would like to ask Dr. Hodes what he thinks of the concept of the computer diagnoses.

Dr. Hodes: I'm very glad that you brought this into focus. Actually, when I called this a metastatic lesion, I demonstrated my stupidity. I was suckered into it because of the age, and I did not take all of the evidence. I talked about the periphery of that lesion, that there was an increase in density around it. That should have put me on my guard. I'm very happy that Dr. Perez-Mesa said something about the computer role. Actually, it performs an extremely important function. It brings to mind many things that we forget; after all, that's the why of all this consulting, to think about things that other people are not thinking about. The difficulty stems from the fact that one has to have a precise glossary of terms. We're going to come up with different answers unless we mean exactly the same thing. Disparities which occur in the computer's diagnoses by no means should dilute our

Fig. 5—Microphotograph of tumor formed by compact cells separated by collagen (x 250).

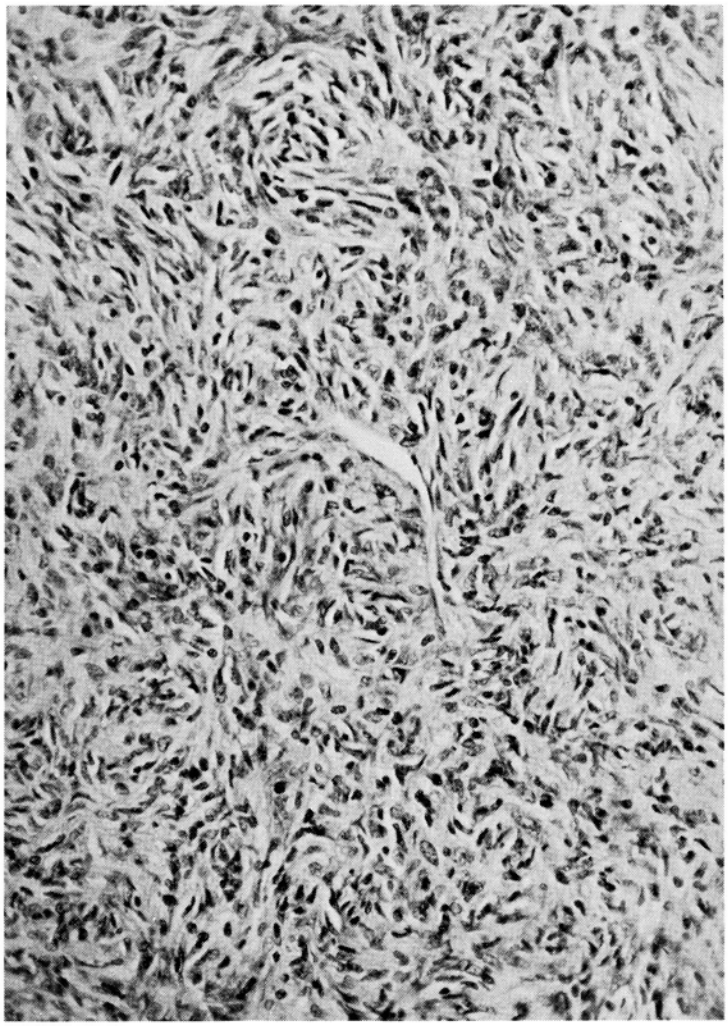
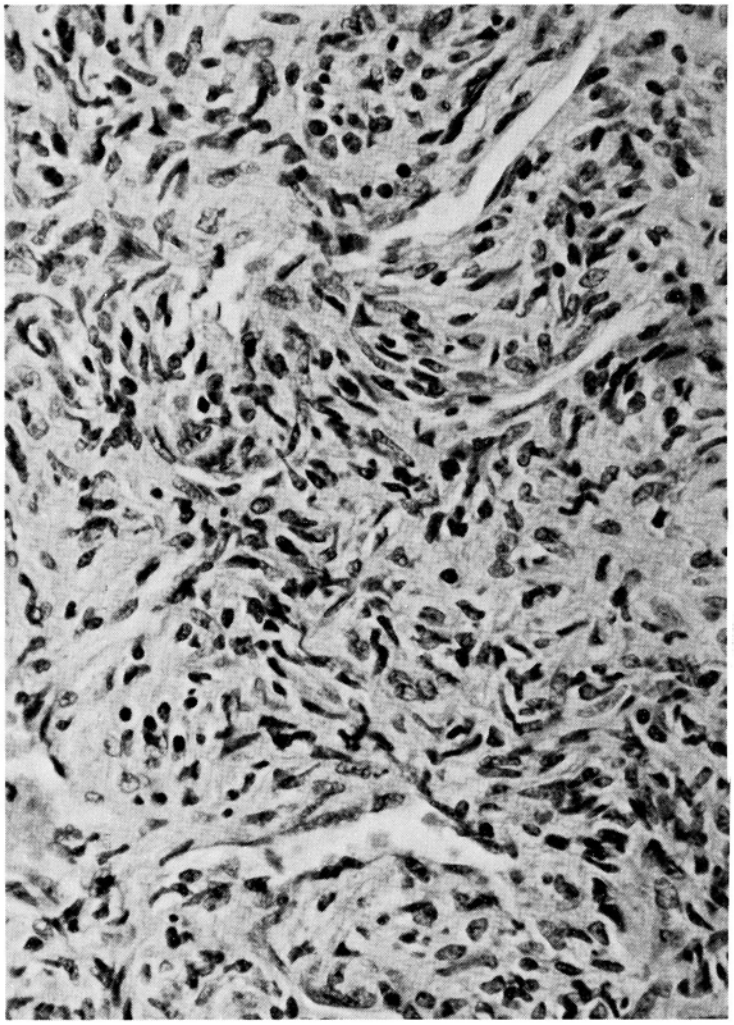


Fig. 6—Higher magnification shows same appearance (x 400).



efforts in that regard. There are many cases in which the computer will bring into focus some things that you never even thought about. Had I seen the computer's printout, which gives you maybe about twenty different diagnoses, and had I studied each one, I might have been somewhat brighter. The day is coming, gentlemen, when we are going to have displays in front of us and we're going to touch buttons which will lead us to another display and finally come to some answers. Someone has to be doing this and I think Dr. Ludwick deserves a great deal of credit.

Dr. Carta: Does the computer directly read off the film or do you have to feed the description?

Dr. Hodes: Actually what you have to do is you have to go through the damndest struggle and I have been through it. Not only do you have to decide whether there's increase in density or decrease in density, but the degree of increase or decrease in density, how much the lesion lies outside the bone, how much of the bone is involved by the tumor in terms of length. I think there's something like twenty to twenty-five parameters that you have to answer, so it is by no means a simple thing: if nothing else, it makes you really look at the lesion and study.

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14. Small-Cell Osteosarcoma of the Distal Tibia

Contributed by **M. H. Levine, M.D.** and **S. Jacobson, M.D.,**
Vancouver, Washington

The patient was a boy, 13 years of age, in December, 1953, when he gave a history of three months' pain in the left ankle, forcing him to limp. There was no palpable mass in the leg; there was right unilateral gynecomastia. The CBC and the urinalysis were within normal limits. The sedimentation rate, at 15-minute intervals, was 2-3-5-8. Blood chemistry tests were not done.

Dr. Hodes: This thirteen-year-old lad complained of pain in his right ankle for three months.

The films are quite inadequate. Indeed, the lateral projection is of no help whatsoever; it is underexposed.

In the anteroposterior projection there is obvious destruction of the lateral aspect of the metaphyseal portion of the tibia. I am unable to see the medullary portion of the bone well enough to form an opinion. There is obviously no periosteal reaction whatsoever.

The character of the erosion is consonant with malignant disease. The only malignant disease I can think of that arises in cortex or periosteum would be an osteolytic osteosarcoma. Certainly metastatic lesions do not act like this. The occasional lymphoma causes pure cortical destruction but almost invariably there is an associated medullary component.

I feel at a distinct disadvantage because of the limited study.

Dr. Hodes' Impression: Osteolytic Osteosarcoma

Radiologic Impressions Submitted:

Ewing's sarcoma	31
Osteosarcoma	29
Fibrosarcoma	09
Metastatic tumor	08
Osteomyelitis	08
Desmoid	07
Neurofibroma	05
Parosteal chondroma	05
Paraosteal osteoma	04
Hyperparathyroidism	04
Reticulum-cell sarcoma	03
Adamantinoma	03
Leukemia	03
God only knows!	01
Twelve others	24

Dr. Hodes: Ewing's sarcoma—I brought it into focus because of age, but I could not see enough of the medullary portion of the bone. Fibrosarcoma is rare. Metastatic tumor is rarer, at this age. There is no reactive bone here to suggest osteomyelitis. Desmoids are usually rather well-encapsulated. I would expect more change in the epiphyseal plate in neurofibroma or hyperparathyroidism. I think this is a malignant tumor; I think it is a sarcoma, and I think that it arises in the paraosteal cortex.

Dr. del Regato: Dr. J. Blumbagen, of Denver, also submitted an impression of osteosarcoma. Drs. R. Chiavarini and S. Chang, of Ann Arbor, and Dr. R. Kilcoyne, of Milwaukee, submitted Ewing's sarcoma. Dr. J. Gutierrez of Tampa, suggested synovial sarcoma. Dr. J. West, Tampa: parosteal sarcoma.

The University of Missouri radiodiagnostic computer diagnosed Ewing's sarcoma.

Operative Findings: In January, 1954, surgical exploration revealed a fungating mass protrud-

ing through the periosteum of the tibia, for about 10 cm. The mass was removed in fragments, which in the aggregate weighed 30 gm; the largest fragment was 3.5 cm in length.

Dr. Dahlin: The case illustrated in case 13 is difficult to classify correctly. I think one should judge by virtue of the cortical destruction of the tibia that this is, in fact, a bone tumor. The cells comprising it are as small as those of Ewing's sarcoma, and that diagnosis becomes highly probable. However, scattered amongst the small round cells are foci in which a pinkish material that one must consider matrix is present. I think it is impossible to say that the matrix produced is not osteoid. The PAS stain really does not help because, although it is positive, it accentuates these areas in which matrix is present. Reticulin stain does not help in differentiation because a fair amount of matrix is produced and it is usually disposed between individual cells.

I think the only differential diagnosis amongst the usually recognized tumors of bone is Ewing's sarcoma and osteosarcoma. Because the matrix seems to be definite I believe this tumor should be called osteosarcoma and sub-typed as small round cell type.

Dr. Dahlin's Diagnosis: Small-Cell Osteosarcoma

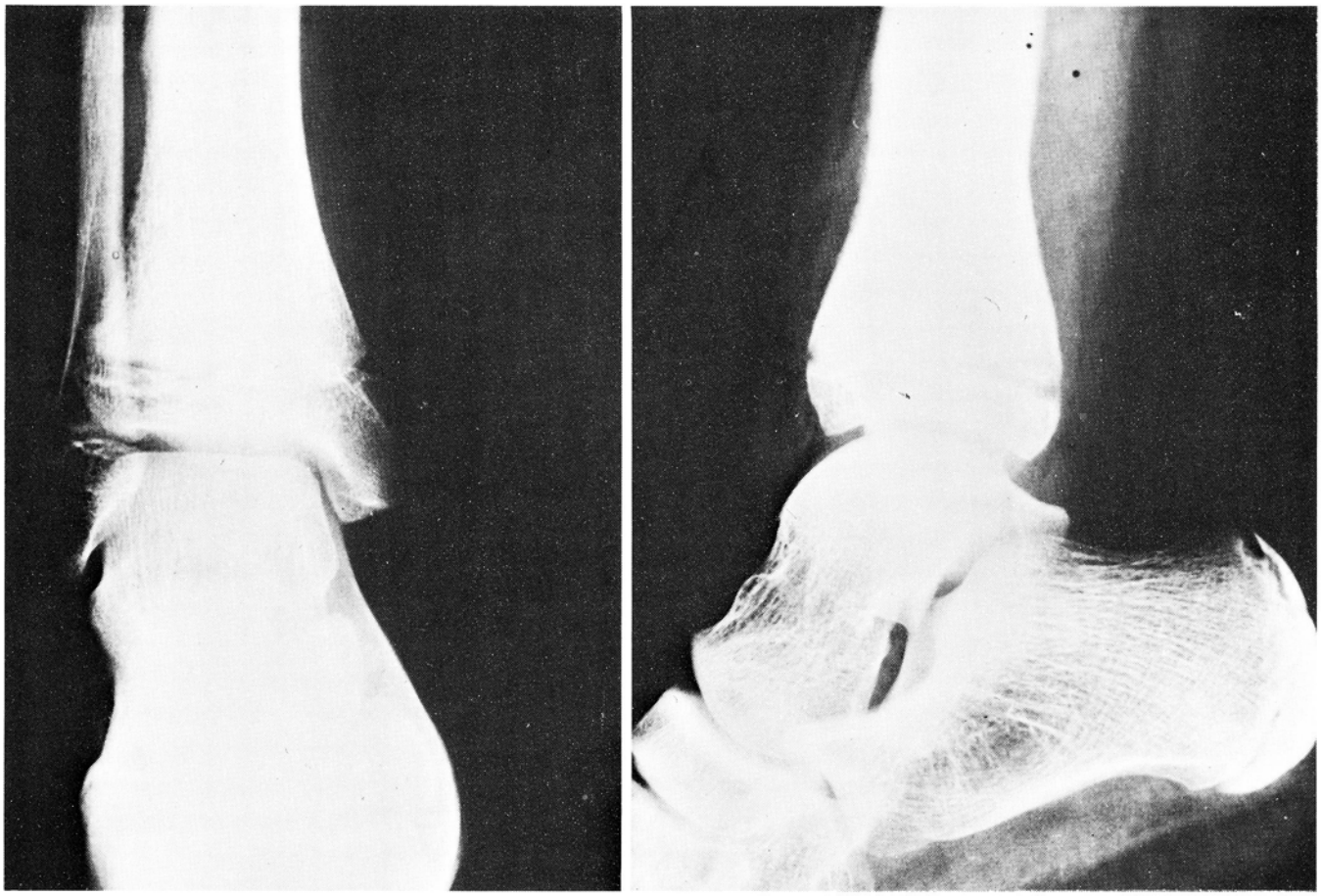
Histopathologic Diagnoses Submitted:

Ewing's sarcoma	50
Synovial sarcoma	25
Reticulum-cell sarcoma	14
Rhabdomyosarcoma	08
Neuroblastoma	08
Others	15

Dr. Dahlin: Some of the participants regarded this as synovial sarcoma. I did not see any second gland-like element in this and I don't think that's correct. I think the cells are too small, too immature, too anaplastic, if you will, for it to be a reticulum cell sarcoma. I did not see anything to make me believe that it should be called an embryonal rhabdomyosarcoma. I don't think it is possible for a metastatic neuroblastoma to have zones with small round cells; I would expect the diagnosis to require that neuroblastoma be ruled out and I would not expect neuroblastoma to produce this osteoid type substance, in any event.

Dr. del Regato: Dr. S. Spanier, of Gainesville, Fla. offered osteosarcoma. Dr. H. A. Sissons, of London, offered a diagnosis of malignant soft tissue tumor. Dr. M. C. Wheeling of Miami called

Fig. 1—The roentgenograms inadequately show a destruction of the lateral aspect of the metaphyseal portion of the tibia.



it metastatic neuroblastoma. Dr. L. V. Ackerman, of Stony Brook, wished for glycogen, connective tissue and reticulum stains but suggested a malignant lymphoma. Dr. M. McGavran of Hershey, Pennsylvania, and Dr. F. Cabanne, of Dijon, France, offered synovial sarcoma. Dr. S. A. Jacobson of Vancouver, Washington, whose case this was, preferred "polyhistioma".

Dr. Lent C. Johnson, AFIP, Washington, D.C., wrote: The x-rays in this case are completely unsatisfactory. One can guess that they were made this way in order to bring out detail that would not otherwise be seen. I would assume that the purpose is to show a saucerizing pattern. This is an undifferentiated round-cell tumor. Since it is a saucerizing lesion and there is some papillary structure, the possibility of a synovial sarcoma can be raised, but there is none of the characteristic biphasic pattern of a synovial sarcoma. A growing tendency that I deplore is to speak of "soft tissue Ewing's tumors"! We have enough trouble already with the misuse of the term as applied to bone tumors.

Dr. Sim: From the clinical standpoint, we would attempt to treat this as an osteogenic sarcoma. If there is confusion in the pathological diagnosis between a small cell osteosarcoma and Ewing's sarcoma, review of the long term survivors in Ewing's sarcoma tends to make us think that an amputation would not be such a bad treatment to control the local lesion. I feel in this case that removing the tumor piecemeal as has been carried out is not adequate cancer surgery. Certainly there are times when one would consider radical en bloc resection of malignant lesions. This is particularly true in low grade primary malignant osseous lesions. Chondrosarcomas because of their slow growth without insidious spread throughout the bone lend themselves to effective treatment by radical en bloc resection. As well, parosteal osteosarcoma and perhaps a new group which we must look at seriously when considering radical en bloc resection is periosteal osteogenic sarcoma. Radical en bloc resection must follow the well established principles of oncological surgery. The entire tumor mass must be removed in an envelope of normal healthy tissue surrounding the tumor. I think that in this case the cortical lesion in this area extending laterally towards the fibula and down into the area of the intraosseous membrane would not lend itself favorably to such a local resection procedure. We would feel that amputation is the treatment of choice in this case.

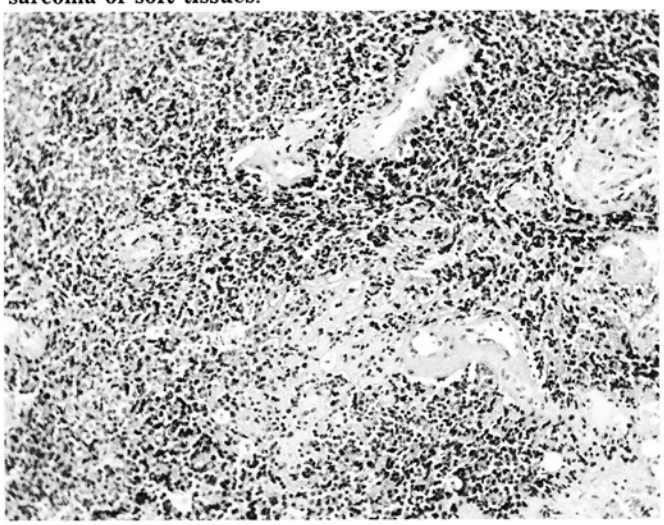
Subsequent History: Following operation, the patient was put in a cast and later received a course of radiotherapy. On August 14, 1954, he expired.

Dr. del Regato: Those of you who are old enough or have a long enough memory may remember the days when it was "square" to call a tumor "round-cell tumor" by the shape or size of the cells that form it; the thing to do, we were told, was to name them after the tissue of origin, their histogenesis, as though we knew!

Dr. Sheldon Jacobson, Vancouver, Washington: I completely agree with Dr. Azar. This is not, I believe, a chondrosarcoma, and I do not believe it's mesenchymal. It's not a chondrosarcoma because most of these cases do not produce cartilage. I don't think it's mesenchymal either—I don't know what a mesenchyme cell looks like, although we speak loosely about it. Some histologists say it's indistinguishable from a fibroblast. Some of them say it's a polyhedral cell. Well, these cells are neither. I don't know what they are and I can identify them in the morula, possibly in the gastrula stage, not beyond.

I first saw this sort of thing in Jaffe's lab about 1933. We had a tumor with small round cells producing bone. Jaffe was puzzled. We don't think of small round cells as producing bone. He finally called it a mesenchyoma, but he was not satisfied. Then I saw one in the late 1940's, at New Haven: small round cells producing cartilage, the sort of thing that Lichenstein and Bernstein, in 1956, called mesenchymal chondrosarcoma. In 1961, Hutter and associates wrote a paper on primitive pluripotential round-cell sarcoma of bone and they pointed out that here was a tumor with small round cells which looked indistinguishable from Ewing's sarcoma, could produce bone, cartilage, vascular tissue, and—according to them—even epithelium, but I am skeptical of the last. It is usually miscalled Ewing's sarcoma. Many of these cases occur after the third decade, so it's not Ewing's. Almost no cases occur in the first decade, so it's not Ewing's. Many of the films, particularly when the tumors differentiate into osteoid, show radio-opaque areas, deeply radio-opaque sometimes. In my series of about three dozen cases, and in the total of reports over 100 cases, about one-fifth occur in the soft tissues.

Fig. 2—Tumor of small cells resembling a Ewing's sarcoma of soft tissues.



It apparently does not matter what treatment we use, whether it's simple excision, resection, amputation, disarticulation, radiotherapy or chemotherapy. You can use one and when the tumor recurs, use another. One is as good as another, so far as we know at the present. More than half of them die after two years, but survival extends all the way up, the extreme being the case that was tumor-free for 19 years, had a recurrence, and died 4 years after that.

Dr. Eduardo Murphy, Mexico City: A good number of participants thought this was a synovial sarcoma. In this type of seminar, the radiologists all get material which is the same for every radiologist, and probably because there is only one or two radiographs—all reproduced in the same way. When you get to the slides, there can be many variations. We had two boxes of slides in Mexico, and I had seventeen very good pathologists look at them, and nobody had any doubt at all that this was a synovial sarcoma, because we had predominantly glandular formation. Unfortunately, Dr. Dahlin did not see this tissue, or at least he did not illustrate it at all, and, therefore, I must assume that this tissue did not show up. I think that this has got to be taken into consideration.

Reference:

Brody, G. L. and Fry, L. R.: Osteogenic Sarcoma: Experience at the University of Michigan. Univ. Mich. Med. Bull. 29: 80-87, 1963.

15. Myeloma of the Bones of the Pelvis

Contributed by **K. Charyulu, M.D.** and **A. R. Morales, M.D.,** Miami, Florida

The patient was a 52-year-old woman in May, 1971, when she complained of progressive discomfort and pain in the right hip, of six years duration; she limped and used a walking cane. At rest, she had no pain. There was a large mass in the right iliac fossa and the right leg was 3 cm shorter than the left. The SMA-12 values were all within normal limits.

Dr. Hodes: We know the complete clinical story on this patient; she comes from our hospital in Florida.

Despite our familiarity with the case, one can make the point that a bulbous somewhat cystic and purely osteolytic lesion in a patient fifty-three years of age must always bring into focus the possibility of multiple myeloma in addition to metastatic disease and fibrous dysplasia. There are such things as huge giant cell tumors and even chondroblastomas into focus. Rarely does fibrous dysplasia assume the proportions of this lesion yet it would have to be considered.

As in all bone lesions, the demonstration of the primary lesion alone does not suffice. Central to the issue is the question as to whether or not the patient has lesions elsewhere in the body.

As we know this patient has had multiple myeloma for many, many years. It may have started as a solitary plasmacytoma which, as is usually the case, at a later time develops other lesions and take on the classical trappings of multiple myeloma.

Dr. Hodes' Impression: Myeloma

Radiologic Impressions Submitted:

Plasmocytoma	38
Fibrous dysplasia	33
Aneurysmal cyst	17
Giant-cell tumor	13
Hemangioma	12
Chondrosarcoma	09
Enchondroma	06
Chondromyxoid fibroma	05
Villonodular synovitis	04
Eight others	10

Dr. Hodes: I am familiar with this case, as it comes from our hospital, but we can make the following radiological points. To begin with, we have a patient fifty-three years of age, which immeditely brings into focus the possibility of metastatic malignancy or multiple myeloma. True, certain metastatic lesions, particularly the kidney, would rank high in differential diagnosis. But far more common, expansile lesions of this character prove to be due to plasmocytoma. Occasionally, one sees a giant-cell tumor that looks like this. Fibrous dysplasia occasionally assumes proportions of this magnitude. Actually, the differential diagnosis is not too difficult if one can be assured that this lesion is monostotic. It so happens I well remember that this patient had a monostotic lesion and the diagnosis of plasmocytoma was made.

Dr. del Regato: Drs. B. Felson, of Cincinnati, A. W. Finestone, of Clifton Forge, Virginia, and R. Arce, of Mexico City, offered myeloma. Dr. R. Mattson, of Denver, preferred hemangioma.

The University of Missouri radiodiagnostic computer diagnosed chondrosarcoma.

Operative Findings: On may 28th, 1971, an open biopsy was done.

Dr. Dahlin: In this instance we have a tumor that historically has been present for 6 years. It has produced some expansion of the bone of origin. Microscopically it seems very easy to "zero-in" on the diagnosis of myeloma. The tumor is composed of closely compacted small round cells. They have the characteristics of abundant cytoplasm associated with rather distinct cell boundaries. The nuclei which are usually eccentric sometimes exhibit a "clock-face" chromatin pattern like that of mature plasma cells. No matrix is present in the material studied.

The differential diagnosis should include any of the small round cell tumors of bone but the cytologic characteristics in this case are different from those of Ewing's sarcoma or malignant lymphoma. Metastatic carcinoma is not a tenable diagnosis because the tumor is not disposed in an organoid pattern and the cytology is that of myeloma.

Dr. Dahlin's Diagnosis: Myeloma

Histopathologic Diagnoses Submitted:

Plasma-cell myeloma 101

Dr. del Regato: As in no other case in this Cancer Seminar, we close on a note of unanimity.

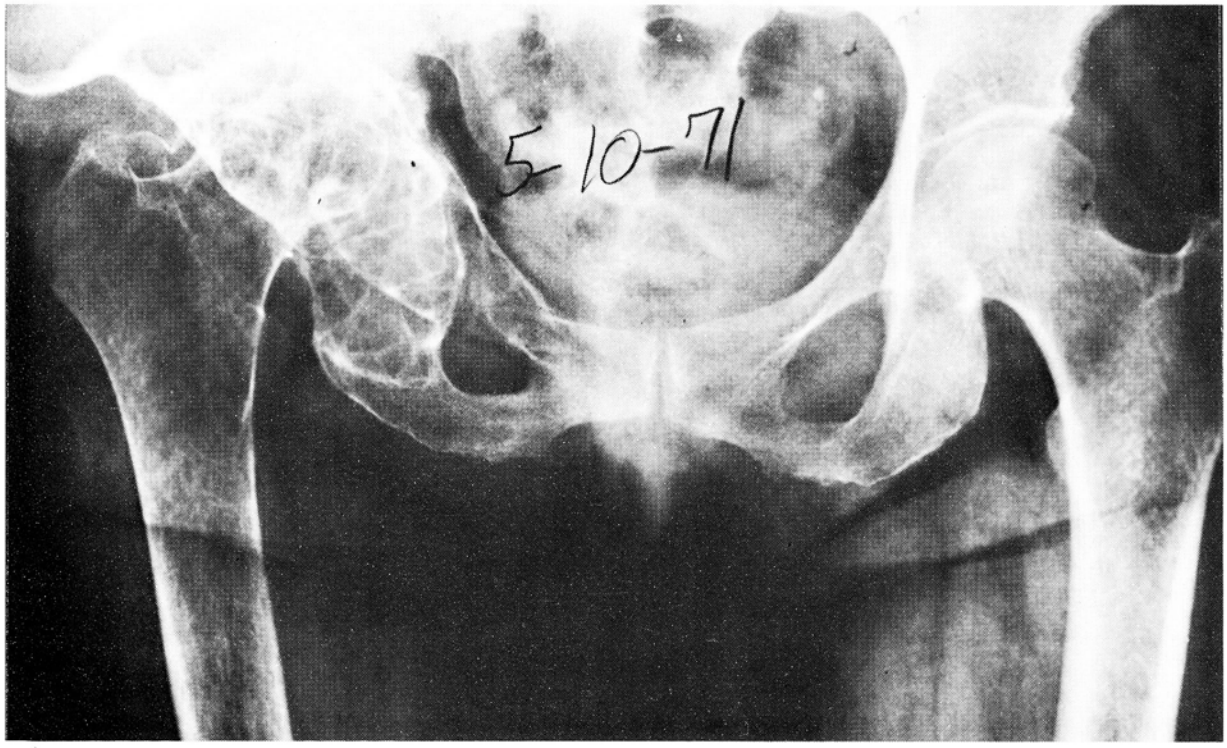
Dr. Lent C. Johnson, AFIP, Washington, D.C., wrote: This is a myeloma. The extensive involvement of one bone raises the possibility of solitary myeloma and the fact that the patient has been walking on it for six years with gradual crumpling of the acetabulum raises the possibility that it is benign. Occasionally, one can distinguish the benign from the large numbers of Russell bodies, but there is not enough material for this distinction.

Subsequent History: Following biopsy, the patient received radiotherapy: a total dose of 4,400 rads was received at the mid plane of the pelvis in 31 days through two parallel opposed fields, anterior and posterior, 21x23 cm in diameter; an additional 800 rads followed in 4 days through slightly smaller fields. The pain disappeared, the mass slowly regressed. On January 7th, 1975, three and one half years after treatment, the patient appeared well, without evidence of recurrence or metastases. (Dr. Charyulu)

Dr. del Regato: Not only the informed histopathologists take good care of absorbing as much information from what they call "x-rays", but also often base their morphologic diagnosis, and even their judgment of varieties of tumors, on clinical and radiographic information, while seeking to support it in some morphologic character that happens to be concommittantly found. This is as it should be, but it is wrong to give the neophyte the impression that the resulting compact was all gleaned through the microscope.

Dr. Sim: This case does not pose any problem of diagnosis to the pathologist but there are considerable therapeutic problems to the physician. With such an extensive trabeculated lesion in-

Fig. 1—Extensive lesion involving the acetabulum, the iliac and pubic bones.



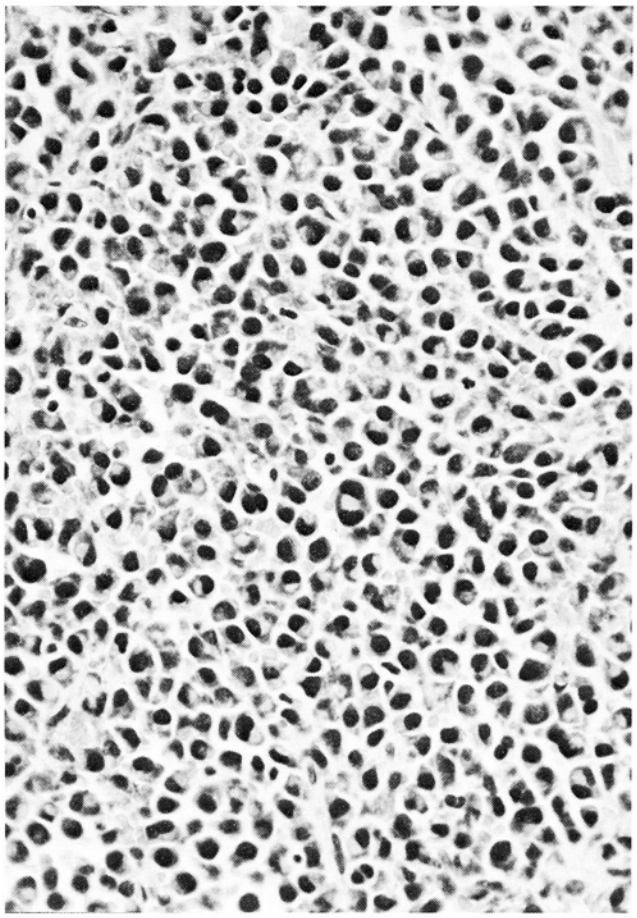


Fig. 2—Typical appearance of myeloma (x 250).

volving the entire right hemipelvis including the hip joint, the surgeon is confronted with problems not only in eradicating the tumor but also in preserving the weight bearing function of the extremity. I would like to reinforce some of the important points that Dr. Dahlin has made in his discussion of the case. Clinical assessment is most important. In the investigation of the patient from the clinical standpoint, it is more important to determine the extent of the disease. In solitary lesions treatment must be very aggressive because many patients live several years before dissemination occurs. Of 34 patients in our series with solitary skeletal myelomas, 18 were alive five years later, seven of these died at intervals from 5-20 years after diagnosis and 11 were still alive at intervals from 7-24 years. In multiple myeloma 2-10 per cent of patients will first manifest their disease as a solitary osseous lesion. However, most will eventually develop multiple lesions of myeloma but their course is often quite protracted. This speaks for more aggressive management of the solitary lesion. I think that in such an extensive lesion involving the hemipelvis as in this case, the treatment of choice will be therapeutic radiation in an attempt to eradicate the local lesion.

Dr. Dahlin: The diagnoses made on this case should be mostly myeloma.

Dr. del Regato: Is this patient free of disease at the present time?

Dr. Charyulu, Miami, Florida: Yes, the last time she was seen, on March 8th, there was no spread of the disease, phoresis, etc. was nomal, so this patient is free of disease at this time.

References:

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Szakacs, J. E. and Carta, M.: Ewing's Sarcoma, Extraskeletal and of Bone. Case Report with Ultrastructural Analysis. Ann. Clin. Lab. Sci. 4: 306-322, 1974.