TUMORS OF THE SKELETAL SYSTEM

THIRTEENTH ANNUAL SEMINAR - 1961

INDIANA ASSOCIATION OF PATHOLOGISTS

David C. Dahlin, M. D., Moderator
The Mayo Clinic

DIAGNOSES

Case 1. Fibrosarcoma of femur
2. Histiocytosis X of skull
3. Neurilemmoma of mandible
4. Giant Cell Tumor of vertebra
5. Osteogenic Sarcoma of femur
6. Fibrous Dysplasia of rib
7. Giant Cell Tumor of femur
8. Chondrosarcoma of ilium
9. Chondromyxoid Fibroma of fibula
10. Osteoid Osteoma of femur
11. Undifferentiated Grade 4 Sarcoma of ilium
12. Ewing's Sarcoma of fibula
13. Desmoid of leg
14. Myositis Ossificans of thigh
15. Malignant Lymphoma, Reticulum Cell Type of humerus
16. Fibrous Dysplasia of rib
17. Hemangiosarcoma of skull
18. Parosteal or Juxta Cortical Osteogenic Sarcoma of femur
19. Osteogenic Sarcoma of fibula
20. Dysplasia, fibrous, of humerus, with cartilaginous islands vs. mesenchymal chondrosarcoma.
Case No. 1

Fibrosarcoma

Variation in size and shape as well as the hyperchromatism of the nuclei in this spindle-cell tumor make it malignant. In the slides that were distributed there was a moderate amount of lymphocytic infiltration which is sometimes seen in fibrosarcoma and other malignant tumors of bone. In addition to the collagenous material there was material in some of the sections that had the appearance of osteoid although this was not definite. Zones such as these, however, might make some wish to classify this as an osteogenic sarcoma of fibroblastic type. Differentiation between fibrosarcoma and osteogenic sarcoma with predominant spindling elements is largely of academic importance only, both tumors being radioresistant. In addition, there were a few foci in which the strands of matrix were undergoing a peculiar form of calcification. This latter feature may be responsible for the densities seen in the central portion of the shaft on the roentgenogram. The roentgenographic appearance, with these densities centrally along with cortical destruction is quite typical of chondrosarcoma, and some chondrosarcomas have peripheral zones that look exactly like high grade fibrosarcomas or even osteogenic sarcoma. Nevertheless there was no evidence of cartilage in any of the sections I examined on this case, Other differential diagnostic considerations include non-osteogenic fibroma and fibrous dysplasia but the nuclear atypias preclude either of these benign diagnoses as does the roentgenogram. The treatment for fibrosarcoma of bone is ablative surgery; usually amputation is required. Contrary to some of the literature, we have found that the prognosis is similar to that for osteogenic sarcoma and not better. Although one-fourth of our cases survived for 5 years, 3 of these 11 cases subsequently died of their tumors so that the long term survival rate was less than 20%.

REFERENCES


Note: In this and the remaining cases of the series, good reference material is found in some of the recent books on bone tumors. These include:


Case No. 2

Histiocytosis X.

This is a classical example of histiocytosis X. (Some still prefer the term reticuloendotheliosis). The group of conditions that are histologically similar include the clinically different (a) eosinophilic granuloma, (b) Hand-Schuller-Christian disease and (c) Letterer-Siwe's disease. The hallmark of the lesion is the histiocyte which ordinarily occurs in sheets as in this case. Eosinophiles vary from few to numerous and generally occur in clusters along with other inflammatory cells such as neutrophils, plasma cells and lymphocytes. Zones of necrosis are relatively common. Mitotic figures may be observed in the histiocytes and this has lead to confusion with malignant tumors. The prognosis varies
with the clinical type, being excellent in eosinophilic granuloma which is ordinarily regarded as a solitary bone lesion (or a few lesions at the most), chronically progressive in the case of H.S.C. and very poor in Letterer-Siwe's. A single lesion of eosinophilic granuloma requires little treatment and some recently have advocated none. Our preference is to treat such lesions with small doses of irradiation. The disseminated forms require complicated therapy. We have been unable to differentiate the subtypes of histiocytosis X on a histologic basis leaving this responsibility to the clinician and radiologist. Differential diagnoses include reticulum cell sarcoma in which the cells are ordinarily much more obviously neoplastic, having hyperchromatism and large nuclei. Markedly degenerating and inflammatory lesions of histiocytosis X, especially in the jaws where secondary infection commonly poses a problem, may be difficult to differentiate from an infectious process. Such cases point up the necessity of adequate, representative material for biopsy.

REFERENCE


Case No. 3

Neurilemmoma.

Neurilemmoma, such as this lesion in the mandible, is an extremely rare tumor in bone. In my original survey of over 2,000 bone tumors there was only one. We have encountered another recently, also in the mandible. In this case the pallisading in areas and the zones with pale staining "foam" cells are characteristic. In addition, the lack of mitotic activity and the circumcision of the tumor are significant evidence of benignancy. Neurilemmomas in bone, as well as those in other tissues, may show marked nuclear variations in size and shape even when benign. A large variety of osseous defects accompany neurofibromatosis but, in few instances is there actual neurofibromatous tissue within bone in this disease. The absence of mitotic figures helps differentiate neurilemmoma from fibrosarcoma. The lack of giant cells and the characteristics on the roentgenogram help differentiate it from fibroma of bone (metaphyseal fibrous defect). Samter, et al have recently presented 3 neurilemmomas and found only 12 others in a review of the literature. They emphasize that it may occur at any age, affect either sex and being benign requires only local removal.

REFERENCES


Case No. 4

Giant Cell Tumor

One should be biased against the diagnosis of giant cell tumor of bone in patients only 14 years old and in lesions involving vertebrae. Even sections
other than those distributed for the conference showed the characteristic features of giant cell tumor throughout. Many multinucleated cells were present in a cellular stroma that was basically not fibrogenic nor osteogenic. The sections did not show evidence for giant osteoid osteoma (osteoblastoma) or for aneurysmal bone cyst, both of which lesions are much more common than giant cell tumors in vertebrae (with the exception of the sacrum). The mononuclear cells of this lesion do not show enough atypia to make one worry about its being a malignant bone tumor with coincidental benign multinucleated cells. It is fortunate that the majority of giant cell bearing lesions in the vertebrae are not true giant cell tumors. Our experience indicates that one can expect a recurrence rate of at least 50% in long term follow-up of giant cell tumors and recurrences in vertebrae would, of course, be extremely serious. In addition, we have noted a 10% rate of sarcomatous change in giant cell tumors. The variants mentioned above have a much better prognosis. The problem of whether radiation should be given to a lesion like this especially if it has not been completely removed is a provocative one. One must weigh the potential sarcomatous and carcinogenic quality of X-ray therapy against the likelihood that part of the tumor is left behind when a vertebra is involved. Perhaps a good plan would be to reserve radiation therapy for those cases in which surgery has proved ineffectual on follow-up. Incidentally, in the older literature on giant cell tumors of vertebrae, most of the reported examples are obviously variants rather than true giant cell tumors in the light of current knowledge.

REFERENCES


Case No. 5

Osteogenic sarcoma.

Approximately one out of every 8 osteogenic sarcomas contains so many benign multinucleated cells that one is tempted to entertain the diagnosis of giant cell tumor. Indeed, the erroneous final diagnosis of giant cell tumor is sometimes made in such cases. Careful study of the cells between the benign multinucleated cells in even the original biopsy specimen in this case, however, show that there is marked nuclear atypia, quite beyond permissible limits for giant cell tumor. Indeed, in some areas of the material available to me there was osteoid being produced by these cells. The final specimen from which the seminar set was obtained shows very obvious evidence of malignancy even though occasional benign multinucleated cells are present. Scattered throughout the final specimen were islands of osteoid production typical of that seen in an osteogenic sarcoma. Strong evidence against giant cell tumor is that this occurred in the shaft of the femur instead of involving the epiphysis as giant cell tumors almost always do. The age of this patient is in favor of an osteogenic sarcoma as opposed to giant cell tumor, but a few (approximately 10%) of giant cell tumor patients are less than 20 years of age. In a study of 430 osteogenic sarcomas in the files of the Mayo Clinic, it was found that 8 had been erroneously classified as giant cell tumors originally and had been treated conservatively.
with disastrous results. In this study which included 53 tumors with a prominent
distribution of benign giant cells throughout, the clinical, roentgenologic and
gross pathologic evidence indicated that such tumors had a much stronger kinship
to osteogenic sarcoma than to giant cell tumor.

REFERENCE

1. Troup, J. B., Dahlin, D. C. and Coventry, M. B.: The Significance of Giant
   Cells in Osteogenic Sarcoma. Do They Indicate a Relationship Between Osteogenic
   Sarcoma and Giant Cell Tumor of Bone? Proceedings of the Staff Meetings of the
   Mayo Clinic. 35: 179 (April 13) 1960.

Case No. 6

Fibrous dysplasia.

The roentgenogram and the microscopic sections in this case indicate that
it is a central lesion that is basically fibrogenic. In addition amongst the
fibroblastic cells, which are producing considerable collagen, there are irregularly
shaped islands of bone which appeared to result from metaplasia of the fibroblastic
cells. All of these features are typical of fibrous dysplasia. In some small
islands there were foam cells which probably resulted from degeneration. The cen­
tral sclerotic part of the lesion is a bit difficult to explain but I believe it has
resulted from healing of prior fracture. On the other hand, certain areas of some
lesions of fibrous dysplasia can be densely ossified and this finding is not
inconsistent with the diagnosis. Occasional lesions of fibrous dysplasia are so
 cellular that one might entertain the diagnosis of fibrosarcoma but this is not a
problem in this particular case. Pallisading of the fibroblastic nuclei in this
case gives the suggestion of neurilemmoma. Rarely one encounters a fibroma in a
rib but fibromas lack the typical zones of osteoid metaplasia seen in this instance.
It is of some significance that in our series, fibrous dysplasia ranked as the
commonest benign tumor of the bones of the thoracic cage. Two-thirds of the
surgically resected tumors of ribs were malignant.

REFERENCE

1. Pascuzzi, C. A., Dahlin, D. C. and Clagett, O. T.: Primary Tumors of the Ribs

2. Lichtenstein, Louis, and Jaffa, H. L.: Fibrous Dysplasia of Bone. Archives of
   Pathology. 33: 777, 1942.

Case No. 7

Giant cell tumor.

In this case, as in case 4, the dominant fields of the tumor are heavily
populated with benign multinucleated cells which are separated by mononuclear
cells with similar nuclear morphology. In neither the original nor in the
recurrent tumors did I find evidence of sarcomatous transformation of this lesion.
Occasional mitotic figures, as in this tumor, are commonly seen in giant cell
tumors that have a benign clinical course. Selected zones within the primary as
well as in the recurrence contain enough fibrous tissue that they could represent
areas from one of the giant cell tumor variants. In cases such as this reference to the roentgenogram, which is typical of that of giant cell tumor, should make one seek histologic material that is unaltered and confirms the diagnosis of giant cell tumor. Foci of osteoid production in giant cell tumors can result from infraction fractures, prior treatment or apparently can even occur spontaneously. The marked tendency of these lesions to recur is demonstrated by this case. Recurrence of giant cell tumor can occur more than 10 years after primary treatment and Jaffe has described malignant transformation more than 20 years following therapy which included radiation. The importance of extremely long term follow-up studies before arriving at conclusions regarding the efficacy of any form of treatment is obvious. We have been unable to grade giant cell tumors thus to indicate their ability to recur or become sarcomatous. As indicated previously, strong evidence suggests that radiation therapy may be important in triggering sarcomatous transformation in this type of lesion. We avoid radiation therapy for giant cell tumors except for the rare ones that are in surgically inaccessible locations. The differential diagnosis of giant cell tumor is not well documented and includes lesions such as: Benign chondroblastoma, chondromyxoid fibroma, giant cell reparative granuloma of the jaws, simple cyst of bone, aneurysmal bone cysts, osteogenic sarcoma, etc. Practically any disease of bone can contain at least focal areas with benign giant cells.

REFERENCE


Note: This reference gives details of long term follow-up studies on 116 giant cell tumors.

Case No. 8

Chondrosarcoma.

This tumor is obviously chondromatous and the only 2 significant differential diagnostic considerations are chondroma and chondromyxoid fibroma, both of which can be almost completely eliminated on the basis of the roentgenographic appearance. The histologic differences between tumors of the chondroma-chondrosarcoma group and chondromyxoid fibroma are illustrated by the next case. Roentgenographically, chondromyxoid fibromas characteristically look benign. The roentgenographic appearance of this tumor indicated that it is an extremely large one and I have not observed a benign chondroma anywhere near this size. The histologic characteristics are well demonstrated. They include a lobular appearance which is constantly found in chondrosarcomas. In the low grade ones, very subtle criteria for malignancy must be employed as outlined by Jaffe and Lichtenstein. These include the presence of more than an occasional binucleated cell, and of cartilage cells with enlarged nuclei. Mitotic figures are rarely found. In this case the number of binucleated forms and the number of nuclei that are larger than those of benign chondrocytes is sufficient to put this tumor "well over the fence" for malignancy. Many chondrosarcomas are soft in consistency and this is reflected in a myxoid appearance microscopically. Whether a chondrosarcoma is firm or soft seems to make little difference in prognosis. All recent studies confirm the fact that wide surgical removal, which often necessitates major amputation, is the treatment of choice for chondrosarcoma. Roentgenologic densities within these tumors result from either ossification of part of the maturing cartilaginous islands or calcification of those that have degenerated. The histologic appearance of chondrosarcoma and its general behavior is the same.
whether it arises secondary to osteocartilaginous exostosis, secondary to endochondroma or is a primary chondrosarcoma.

REFERENCES


Case No. 9

Chondromyxoid fibroma.

Sections of the case illustrated in the roentgenogram as well as those from a substituted case which some of you received because of a shortage of material are basically similar. The tumor is composed of lobules, some of which have fused, of a fibromyxocartilaginous tumor in which are a few cells with large and "worrisome" nuclei. These characteristics are those of the tumor that Jaffe and Lichtenstein first described and called chondromyxoid fibroma--a tumor apt to be mistaken especially for chondrosarcoma. The roentgenogram is typical in that it looks benign. In some areas of this tumor the stroma between the lobules of chondromyxoid substance contains benign giant cells and in a few areas cells that resemble the stromal cells of benign chondroblastoma. As previously indicated, the roentgenographic appearance is that of a benign tumor and this is an important adjunct in the diagnosis of chondromyxoid fibroma. These tumors vary somewhat from case to case containing variable amounts of chondroid, fibromyxoid and myxoid substance. Some of them contain a fair amount of tissue that resembles chondroblastoma indicating a strong relationship between these two benign tumors. Occasional chondromyxoid fibromas recur but none has been described as having undergone malignant transformation. The fact that even benign tumors such as this one may recur following curettage emphasizes the wisdom of doing excisional biopsy whenever possible such as in this fibular lesion, in a rib or in an eccentric cortical lesion in a major bone.

REFERENCES


Case No. 10

Osteoid osteoma.

I was particularly interested in including this example of osteoid
osteoma because the x-ray is rather typical of this tumor but the histologic appearance is somewhat atypical. In this lesion (unless it was different on the slides from the substitute case which some of you received) the osteoid trabeculae are larger, longer and more loosely arranged than in the average osteoid osteoma. In addition it is more vascular than average. These are features suggestive of the tumor that has been called giant osteoid osteoma (benign osteoblastoma). It is cases like this that make me feel that osteoid osteoma and osteoblastoma are closely related entities. In any event, the lesion is well demarcated from the adjacent bone and the osteoblasts which are prominent and mantle the osteoid trabeculae of the tumor are manifestly benign. The ordinary osteoid osteoma apparently has a very limited growth potential and is rarely more than a centimeter or two in greatest diameter. Those lesions with this looser and more vascular structure, however, may grow to a much larger size and occasionally the cellularity of these so-called giant osteoid osteomas are such that one might entertain the diagnosis of osteogenic sarcoma. It is of some interest that although the American literature tends to rather sharply separate the ordinary osteoid osteoma from the giant osteoid osteoma (osteoblastoma), the European literature tends to include lesions of all sizes with this general histologic pattern under the term of osteoid osteoma.

REFERENCES


Case No. 11

Undifferentiated grade 4 sarcoma.

This tumor is one of the most difficult of the series and I am not sure that I can categorize it exactly. It is obviously highly malignant, made up of fairly uniform cells and shows areas of necrosis. In our study of Ewing's sarcoma which is made up of small round cells, we encountered a group with somewhat larger cells than the average Ewing's sarcoma. This group with larger cells was so similar in clinical features and bad prognosis to the remainder of the Ewing's that we lumped them with the Ewing's sarcomas. In this case, however, it seems that the cells are even larger than they are in that group of tumors that we have chosen to call large cell Ewing's sarcoma. This tumor makes one think of the type of osteogenic sarcoma that Aegertor and others have included amongst the osteogenic sarcomas because of the nuclear similarity of these tumors to those of other osteogenic sarcomas even though no osteoid is produced in them. It becomes an academic problem, in this particular case, since there apparently is no satisfactory surgical manner of treatment in this location. In an extremity where amputation would be the treatment for radioresistant tumor I would be afraid to depend on radiation for this lesion because of the large size of the nuclei. This tumor does not have cytologic features that make me believe it belongs in any portion of the malignant lymphoma category.

REFERENCE

I know of no specific references that helps solve this particular problem.
Case No. 12

Ewing's sarcoma.

The highly anaplastic small round cells of this malignant tumor are typical of Ewing's sarcoma. The tumor cells have shown their capability of invading by permeating amongst muscle bundles and perhaps into small vascular spaces. The tumor cells occur in large clumps with little or no stroma within these islands of cells. The nuclei do not have characteristics of cells in the malignant lymphoma series of tumors. We regard it unsafe to consider the diagnosis of reticulum cell sarcoma (primary malignant lymphoma) of bone unless one can say with assurance that the cytologic features of the cells make the tumor fall in the malignant lymphoma series. One must accept the possibility that a highly anaplastic small cell tumor such as this can represent a metastasis from some obscure primary. In actual practice, however, if no source is found for a tumor such as this it is necessary to treat it on the assumption that it is primary in the bone. As indicated previously a few highly undifferentiated primary tumors of bone contain cells somewhat larger than those in this case which are classical of Ewing's sarcoma, but the clinical features of this smaller group of tumors with larger cells is so similar that it seems feasible to include them with the Ewing's. In a recent study of 165 cases of Ewing's sarcoma we found, to our surprise, that there was a 5 year survival rate of 15% and the tumors in the survivors looked fundamentally like the tumor under discussion. To our further surprise, 6 of the 20 survivors died more than 5 years, and two more than ten years, following the initial therapy. Subtracting these delayed deaths from the overall group, we still had a cure rate of approximately 10%. We could arrive at no firm conclusion as to whether radiation or amputation was unequivocally the better form of treatment but amputation seemed to hold a slight edge. The patient represented in case 12 was alive and well when last heard from nearly 2 years after amputation of the leg just above the knee.

REFERENCE


Case No. 13

Desmoid.

This markedly fibrogenic tumor of the soft tissues constitutes an interesting problem. It has some fairly cellular areas in which a rare mitosis can be found, but overall it shows well differentiated fibroblastic cells. The tumor is obviously not encapsulated as evidenced by its periphery where it is invading along the fascial planes and into skeletal muscle. In at least some of the sections there are characteristic giant cells produced by degenerating muscle fibers that are being invaded by the tumor. Overall, these features are those of extra-abdominal desmoid tumors. In contrast to most frank sarcomas which are usually well delimited by a pseudo capsule this type of tumor has a poorly defined and invasive border. This lesion has practically no tendency to metastasize but a strong tendency to local recurrence unless the entire area affected, as for instance an involved muscle, is completely excised. Some people have called this type of tumor a non-metastasizing fibrosarcoma, but we prefer the term extra-abdominal desmoid because of its reluctance to metastasize. Extra-abdominal desmoids, especially those that are recurrent, may invade structures that make them so painful or make the extremity so useless that amputation becomes necessary.
REFERENCES


Case No. 14

Myositis ossificans.

The histologic appearances in this tumor is characteristic of the florid phase of myositis ossificans, a lesion that has been commonly misdiagnosed as osteogenic sarcoma. As described by Ackerman, these peculiar reactions in the soft tissue tend to have a peripheral rim of maturation to bone. This is evident in this example. The central part of the lesion is composed of extremely cellular fibroblastic tissue that contains mitotic figures. The nuclei of these proliferating cells, however, are not dysplastic, and one can trace these cells into rather orderly trabeculae of bone. Sometimes a chondroid phase is interposed between the strictly fibrous and the bony elements. A history of trauma, as in this case, is a clue that the lesion is of this reactive type but a history of trauma is not always obtained. The rapid growth is typical. The extra-osseous location with rarely any change in the bone itself (unless there has been extremely deep trauma) is likewise typical. The tumor bears some resemblance to the benign subcutaneous lesion called pseudosarcomatous proliferative fasciitis which does not tend to become ossified.

The smoothly outlined benign appearing proliferative lesion on the shaft of the femur in this case would seem to be completely unrelated to the process under discussion.

REFERENCES


Case No. 15

Malignant lymphoma, reticulum cell type.

The histologic appearance in this tumor are typical of reticulum cell sarcoma of bone. The cells are disposed in an alveolar arrangement, that is in clusters and columns separated by strands of stainable reticular material. This is in contrast with what one sees in Ewing's sarcoma where large clusters of cells are seen characteristically in the absence of such material. In addition, the nuclei for the most part show the indentation typical of reticulum cells, and they have a cytoplasmic border that is indistinct. Another feature is involvement of regional lymph nodes which is more commonly seen in reticulum cell sarcoma than in any other tumor of bone. The roentgenogram in this case is typical in that it demonstrates features of a malignant tumor but does not indicate very strongly the histologic type. I have come to prefer the term malignant lymphoma to reticulum
Case No. 15 (continued)

cell sarcoma of bone as originally advocated by Parker and Jackson because one sees such great variation in cell type. Most malignant lymphomas in bone are composed predominantly of reticulum cells but many of them have an admixture of lymphoblasts and lymphocytes and some are even predominantly lymphoblastic or lymphocytic. Even Hodgkin's disease can, on rare occasions, present as a primary tumor in bone. Clinically, patients with lymphoma in bone may have this as their primary and only recognizable disease. They may, however, show evidence of involvement of other tissues including especially lymph nodes. Finally, the osseous involvement may occur as a late manifestation of a proved malignant lymphoma or even a leukemia. When a patient's malignant lymphoma appears to be primary in bone and no other disease found, the chance of cure is somewhere between 30 and 50%. No firm stand can be taken regarding the best treatment for this disease; the weight of evidence perhaps favors radiation except for those tumors easily amenable to treatment by amputation.

REFERENCES


Case No. 16

Fibrous dysplasia.

This example of fibrous dysplasia shows most of the features previously enumerated for this process. In addition, it contains zones in which there are fairly numerous benign giant cells. These occur in some examples of fibrous dysplasia apparently as a response to degeneration within the lesion. This lesion exhibits myxoid degeneration and micro-cyst formation. This brings up the point that occasional examples of fibrous dysplasia are partially or even predominantly cystic. Sections from the degenerating central parts of such lesions are not necessarily diagnostic of fibrous dysplasia, but appropriate sections from the peripheral regions ordinarily show the characteristic fibrous tissue and metaplastic osteoid that clinch the diagnosis. The histologic sections in this case demonstrate the expanded and attenuated cortex of the affected rib and show that the process has not perforated into surrounding tissues. Foci of fibrous dysplasia are basically the same whether they are monostotic, polyostotic or the relatively rare form of polyostotic fibrous dysplasia that is associated with Albright's syndrome which includes precocious puberty, marked predilection for females, dwarfism and areas of brownish pigmentation of the skin. Fibrous dysplasia is only extremely rarely followed by sarcoma, being less than a dozen cases in the literature. We have studied 4 examples of fibrous dysplasia that were followed by sarcoma in the same region. All of these patients had radiation therapy to the original benign disease which in each instance was in a jaw. Further, there is little or no evidence that radiation is efficacious for the treatment of fibrous dysplasia.

REFERENCE

Case No. 17

Hemangiosarcoma.

In the sections distributed, the hemangiosarcoma is somewhat masked by the hematopoietic marrow which it was permeating. In other sections from this case it is more obvious that this is an angioblastic tumor. Hemangiosarcoma primary in bone is rare. Dr. Jaffe, in his book, mentions that they may be multicentric or at least appear to be multicentric as in this case. I have encountered only one similar example and it involved simultaneously several bones. It is interesting that in this case, as in mine, the sections show, in several areas in the skeleton, cavernous spaces that appear completely benign but are associated with spindle sarcomatous elements. This suggests a multicentric origin for the disease. It is no longer commonly felt that Ewing's sarcoma represents a hemangioendothelioma. In any event, it is quite different from the case under discussion. Among the vascular tumors of bone one must include hemangiopericytoma which is also extremely rare. Hemangioma is stated by the roentgenologists to be relatively common, but these tumors of the skeleton are rarely operated upon.

REFERENCE


Case No. 18

Parosteal or juxta cortical osteogenic sarcoma.

From the roentgenographic evidence this is obviously a large, bone-forming tumor. Lateral views of the lower part of the femur showed that it was a tumor external to the bone. The microscopic section distributed showed that the periphery of the tumor was enveloping striated muscle fibers much in the manner of a desmoid tumor. The basic proliferating cells are fibrogenic but are undergoing metaplasia and producing bony trabeculae. In this instance the spindle cells are manifestly malignant with fair numbers of mitotic figures and considerable nuclear anaplasia present. In some of these parosteal osteogenic sarcomas the spindle cells are much better differentiated. Even with minimal evidences of malignancy in the presence of a characteristic roentgenogram the diagnosis of parosteal osteogenic sarcoma can be made. The important differential considerations include myositis ossificans, the features of which have already been described. The roentgenogram affords almost diagnostic differential features. Another condition to be differentiated is osteochondroma (osteocartilaginous exostosis) but this tumor has a cartilaginous cap and the bony trabeculae are separated by either fat or hematopoietic marrow instead of the fibroblastic tissue of parosteal osteogenic sarcoma. Rarely a subperiosteal ossifying hematoma can produce somewhat of a problem but it lacks nuclear anaplasia and shows peripheral maturation to bone in contrast to what one ordinarily sees in parosteal osteogenic sarcoma where the periphery is the most fibrogenic and proliferative part. Although some surgeons attempt to remove a parosteal osteogenic sarcoma by block excision the consensus is that, for any but very small and non-recurrent tumors, amputation is the treatment of choice. The patient under discussion was subjected to amputation at the time of the second operation and he finally succumbed to pulmonary metastasis more than 6 years after the amputation and 13 after the onset of symptoms. Nearly 1/3 of our patients with parosteal osteogenic sarcoma
have eventually died with metastases attesting to its serious nature. Several of those that succumbed with metastases have had recurrent tumors of increased degree of malignancy.

REFERENCES


Case No. 19

Osteogenic sarcoma.

This, even though some of the slides distributed had little tissue on them, seems to be a very straight-forward osteogenic sarcoma. Although the nuclei are a bit small they are distinctly irregular in size and shape and some of the larger ones have prominent nucleoli. The lace-like pattern of osteoid that has been produced by these malignant cells is so characteristic of osteogenic sarcoma that it-in itself-is almost diagnostic. The bluer staining osteoid trabeculae are those that have some mineralization. Some of the slides in this case contained a few benign giant cells which again have no significance but may add confusion. In some areas, rather large blood-filled spaces are present. Osteogenic sarcomas with these spaces have sometimes been called telangiectatic osteogenic sarcomas or malignant bone aneurysms. We have no evidence to suggest that the finding of large blood spaces has any significance in osteogenic sarcomas. On occasion they may make one worry about the possibility of the lesion being an aneurysmal bone cyst.

I would like to make a plea for amputation, as early as practicable, in patients with osteogenic sarcoma. I know of no reliable statistics to indicate that any other form of treatment is better or even as good. In our experience, nearly 20% of patients with osteogenic sarcoma survive 5 years when treated by amputation, and 15% survive 10 years.

REFERENCES


Case No. 20

Dysplasia.

Dr. Pontius said in his original communication regarding this group of cases that the diagnosis in this one may be "a guess". This is an extremely unusual and interesting lesion and I have never seen one quite like it before. I believe that
the evidence in the sections I had to study indicates that the process is a bizarre dysplasia of bone. There are numerous zones in which rather regular cartilaginous islands simulated epiphyseal lines and exhibit enchondral ossification. I believe these are reflected in the roentgenogram. In addition, there are zones rather typical of fibrous dysplasia. There is one area in which the spindle-cell component is extremely active and shows fair numbers of mitotic figures, but I do not believe this area is malignant. It probably represents a healing reaction. I am biased against the possibility of malignant transformation because, in my interpretation, this is a complex dysplasia of bone, and I am leaning on the fact that dysplasias in bone have very little potential towards malignant transformation. The Journal Bone and Joint Surgery for December 1960, page 1329 does, however, illustrate a somewhat similar case in which multiple lesions, at least some of which had histology similar to this one, were present and sarcoma developed. I have seen a few examples of dysplasia in which prominent cartilaginous components tended to obscure the classical zones of fibrous dysplasia.

REFERENCE

List of Diagnoses to be sent to: David C. Dahlin, M. D.
The Mayo Clinic
Rochester, Minnesota.

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INDIANA ASSOCIATION OF PATHOLOGISTS

THIRTEENTH ANNUAL SEMINAR

TUMORS OF THE SKELETAL SYSTEM

presented by:

David C. Dahlin, M. D.

The Mayo Clinic

Date: May 21, 1961
Time: 10:00 a.m. (C.D.T.)
Place: Veterans Adm. Hospital Auditorium,
    1481 West 10th Street,
    Indianapolis, Indiana.

Sponsored Jointly by:
    Indiana Ass'n. of Pathologists
    U.S. Veterans Adm. Hospital
    Methodist Hospital
LIST OF DIAGNOSES FOR YOUR FILE

Case No. 1.

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Case No. 1

Indiana University, Indianapolis
Accession No. 87439

The patient was a 65 year old woman. She was admitted to the hospital because of sharp pain in the distal part of the right thigh. The pain began 3 weeks prior to admittance, was dull in character, but persisted. The roentgenograms revealed osteolytic changes of the distal third of the femur with amorphous densities in the medullary canal, rarefied cortical surfaces and extensive periosteal calcifications. A biopsy was performed. The sections are from the subsequent amputation specimen, no tissue remains from the biopsy specimen.

Case No. 2

Indiana University, Indianapolis
Accession No. 86192

This 3 year old white boy has had a chronic discharge from the left ear for 8 or 9 months. Multiple incisions and drainage of the area have been performed. At the time of mastoid biopsy, soft tissue extending from the middle ear to the occipital bone was found.

Case No. 3

Indiana University, Indianapolis
Accession No. 99435

A 20 year old negro woman was first seen at the Indiana University Medical Center with complaints of swelling of the left side of her jaw of one year duration. Following the extraction of the left mandibular third molar, she had gradual onset pain and swelling in that region. In addition, she stated that for nine years she had noticed two small nodules within the left nostril. The left mandible presented with a hard moderately tender mass near the ramus. This extended both medially and laterally. The nostril lesions were firm and measured 1.5 and .3 cm. in diameter. The hemogram consisted of 8.8 gms. per 100 ml. hemoglobin; 3.17 million RBC; 6,400 WBC with 53% neutrophils, 27% eosinophiles, and 15% lymphocytes, and 6% monocytes. The platelet count was 662,530. The sternal bone marrow appeared hyperplastic without diagnostic features. Roentgenograms revealed a large region of destruction involving the ramus, angle, and posterior portion of the body of the left mandible with partial resorption of the roots of the second molar and an expanded thinned cortex. No explanation was found for the patient's anemia which was treated by blood transfusions. After biopsy, the left mandible was explored by a cutaneous route. Approximately 90 gms. of tissue was removed leaving a 4 X 5 cm. cavity. This was considered an incomplete removal at the time. At two separate subsequent operations, additional tissue was removed from the mandible. The nodules from the nostril were likewise removed. With continuance of pain and swelling in the region of the angle of the mandible, additional tumor was resected by an intra-oral approach. Finally, resection of the mandible including the ramus and a portion of the body was performed, some six years subsequent to the original admission.
Indiana University, Indianapolis  
Accession No. 81563

This 13 year old white boy had a history of weakness of the lower extremities for several weeks. No bladder or bowel symptoms were noted. On examination, low back pain was elicited. Complete block at the level of D-12 was demonstrated in the myelogram. Laminectomy with partial removal of an epidural tumor was performed.

Terre Haute Medical Laboratory  
Accession No. ST-59-2188  
ST-60-721  
ST-60-819

This is the case of an 18 year old girl who had complaints of soreness in the right leg and right knee of one month's duration. Swelling of the knee was noticeable seven days prior to hospitalization. Roentgenograms revealed a lesion described as a large cystic area in the shaft of the femur, six inches proximal to the knee. An operation at this time consisted of curetting and packing of the cyst. Roentgenograms later revealed a mild new periosteal reaction. One month later, severe pain was experienced. Roentgenograms revealed a pathologic fracture through this area. A second biopsy was obtained. This was followed by amputation.

Methodist Hospital, Indianapolis  
Accession No. 7083-57

A 53 year old white male was examined because of complaints of bronchial cough and fatigue. A routine roentgenogram of the chest revealed a tumor of the right eleventh rib. No symptoms were elicited in regards to the rib lesion, although he did have complaints of pain in the upper dorsal region, especially noted at times of fatigue or being overly tired. A segment of the rib containing the tumor was resected.

Methodist Hospital, Indianapolis  
Accession No. 3976-58  
2719-60

This 26 year old woman had complaints of generalized soreness in the region of the left knee for approximately one year. Recently she had noted swelling
of the left knee, on the inner side. Minimal weakness of the left knee was also mentioned. Weight bearing had been possible throughout this period of time. Roentgenograms revealed a rarefied area involving the medial condyle of the left femur. It was stated that two years previously, she had bruised the left knee at the time of an automobile accident, which, however, did not require hospitalization and which the patient described as being not a severe injury, and as not producing disability. Examination revealed slight swelling over the medial condyle of the left femur with slight tenderness to palpation. Routine laboratory work produced results within normal limits. The alkaline phosphatase was 1.2 Bodansky Units with 1.6 mgs.% phosphate. The serum calcium was 10 mgs. per 100 cc. An operation was performed consisting of curettage of tumor area and packing of the residual cavity after phenolization with bone chips from the left ilium. Two years later she was re-admitted following a fall in which she sustained injury to her left knee. However, she complained of occasional tenderness in this area over the last six months. Recent roentgenograms revealed an increasing osteolytic area in the region of the previously curetted tumor. Laboratory studies at this time revealed hemoglobin levels of 10.5 to 11.7 gms.%; WBC from 7,950 to 10,900; essentially normal urinalysis; an alkaline phosphatase of 1.2 Bodansky Units with a phosphorus of 3 mgs.%. At surgery the entire osteolytic defect was curetted until all recognizable pathologic tissue was removed. After frozen section study the defect in the condyle was again packed with bone chips from the ilium.

Methodist Hospital, Indianapolis
Accession No. 6592-60

This 26 year old man was admitted with chief complaints of progressive swelling of the right hip over the past year. The patient has known of multiple tumor masses present near metaphysial areas of nearly all long bones, scapulae, and both ilia throughout his life. Early in his life he reported the growths did increase in size but had stabilized with very little change since early adulthood. The swelling in the right hip area is an exception to this. He gives a history of continually irritating this bony outgrowth, especially when pitching softball. Persistent intense discomfort in this area was present in the past year. He reported no skin discoloration or increased temperature over this area. Past history reveals that the patient's grandfather and the patient's one and only daughter present with multiple tumors similar to his own. None of these relatives, however, have experienced any complications in regard to the tumors. Physical examination was within normal limits except for the presence of the multiple tumor masses near the metaphysial ends of nearly all long bones. None were tender. The right iliac mass was large, firm, and extended from the anterior superior spine posteriorly to the sacroiliac articulation. It extended from the iliac crest superiorly to the greater trochanteric area inferiorly. Localized tenderness over the midportion of the posterior aspect of this mass was present. The skin appeared to possess increased temperature. Striae were present overlying the mass with a prominent venous pattern in the skin. Limitation of motion of the right lower extremity was present and motion produced discomfort. Routine laboratory studies revealed an essentially normal hemogram; a few casts without albuminuria in the urine; an alkaline phosphatase of 3.6 Bodansky Units; and a 4.8 mgs.% phosphorus level. At time of operation, the cartilagenous mass appeared well encapsulated. It was resected along with the osseous pedicle at its base.
Methodist Hospital, Indianapolis
Accession No. 84L7-56

Case No. 9

This 8½ year old white girl was admitted because of the presence of the tumor at the proximal end of the right fibula. A history of injury four months previously was elicited, at which time the patient tripped and fell over a log. No skin lesion occurred, however. The tumor, however, had been noticed since this time of injury. Remaining history and physical examination revealed no abnormalities except for a globular mass involving the proximal metaphysis of the right fibula which could be palpated laterally and which was described as rubbery or fluctuant in nature. Slight discomfort was elicited on pressure. At surgery the tumor mass was found to be discrete and covered by thickened periosteum. Excision of the tumor was done by resection of the proximal one-third of the fibula leaving the proximal epiphyseal line and articular surface.

Methodist Hospital, Indianapolis
Accession No. 1685-58

Case No. 10

A 21 year old male was admitted following one and a half years of soreness in the left hip. For the past five months the hip continued to be sore during the day but ached at night, frequently sufficiently severe to wake him up and force him to arise. There was no great amount of disability nor was limp produced. Increased activity did not cause increased discomfort nor did rest give improvement. The only traumatic history was two months previously when he was accidentally stabbed with a knife four inches above the left knee. Roentgenograms were taken one month prior to admission. A block resection of the area was performed from the region of the lesser trochanter up this left femur.

Methodist Hospital, Indianapolis
Accession No. 1082-58

Case No. 11

A 22 year old white female was admitted with complaints of pain in the region of the right hip progressing down the right leg and the right sacro-iliac area for the previous four months. No trauma history was elicited. Over this four month period of time several X-rays were taken in different laboratories and interpreted as showing no abnormalities. Coughing and sneezing aggravated the pain. She also experienced anorexia and weight loss of approximately 40 pounds during this period. The pain was severe enough to require Demerol for relief. The past history was negative. She had also noticed weakness and loss of energy. Physical examination revealed a young dark complexioned, actually dusky woman who appeared in obvious discomfort and ill. The complexion was poor, with acne and comedones. The skin showed evidence of considerable recent weight loss. Palpation of the abdomen suggested possible enlargement of the right kidney. A hard mass was palpable in the right lower quadrant which appeared fixed to the pelvis and extended above the pelvic brim posteriorly for 2 inches. Pain was elicited on extreme flexion, abduction,
and external rotation of the right hip with weakness of the gluteus maximus and minimus and spasm of the maximus. Tenderness was present over the sacro-iliac area on the right. Posteriorly the mass could be palpated. It did not extend beyond the mid-line. Laboratory examination revealed a hemoglobin of 11.2 gms, of hemoglobin, 33% hematocrit, and a WBC of 12,900 with 92% polys and 8% eosinophiles. Urinalysis revealed a very faint trace of albumen, a faint positive occult blood test, 10 - 15 WBC per h.p.f., and 8 - 10 RBC per h.p.f. No Bence-Jones protein nor melanin could be identified in the urine. A blood urea nitrogen was 5 mgs.%; a total protein was 5.7 gms.% with albumen 3.33 gms. and globulin 2.37 gms. for an A/G ratio of 1.4 - 1. The alkaline phosphatase was 6 Bodansky Units with phosphate 3.9 mgs.%. Mantoux tests were negative. Sedimentation rate was 26 mm. by the Cutler Index method. The serum calcium was 8.4 mgs.%. Serum protein electrophoretic studies revealed a decrease in albumin and increase in alpha\textsubscript{1}, alpha\textsubscript{2} fractions of the globulin. An open biopsy of the lesion of the right ilium was undertaken.

The Mayo Clinic
Accession No. C3503-61

A 10 year old girl registered with the complaint of pain in the left fibular region of one week's duration. A diagnosis of osteomyelitis had been made and she had been treated with penicillin. Examination revealed a tender swelling in the mid portion of the left fibula. A roentgenogram revealed a destructive lesion in the same region.
Case No. 13

Methodist Hospital, Indianapolis
Accession No. 8247-56

A 25 year old married white male presented with chief complaint of a mass in the region of the calf of the right leg. Past history revealed that the mass had developed in the calf of the leg two years previously at which time it had been removed. Subsequently the patient had developed an infection in the leg in this area and one year previously appeared to definitely have had a recurrence of the tumor. A second excision was performed at this time. The current admission was for local excision or amputation. The only traumatic history was a power mower injury to the toes of the right foot. Physical examination revealed a well developed, well nourished intelligent man. Physical findings were essentially normal except for the firm mass palpable in the calf of the right leg. Routine laboratory work showed normal results. After preliminary biopsy and pathologic examination, an amputation was performed. Dissection of the amputation specimen revealed a multi-nodular tumor mass measuring 9 x 9 x 18 cm. involving the upper portion of the leg. Previous X-ray examination had revealed no osseous involvement.

Case No. 19

Methodist Hospital, Indianapolis
Accession No. 5790-60

A 31 year old white male stated that approximately 6 - 8 weeks previously he had bumped his right leg on the edge of a table. The skin turned black and blue but healed up and presented no additional discomfort. Three weeks prior to admission the patient experienced left leg pain and it appeared to swell. Analgesics were administered and a trial of ultrasound therapy produced more pain and actually difficulty in walking. X-rays were then taken and interpreted as negative with the exception of an old bone infection, according to the patient. The pain is described as an aching type of sensation that centers in the right thigh laterally but which would radiate to the ankle. The pain was worse at night. No type of position produced relief from the pain. No other history of injury except to the second digit of his left hand was elicited. The patient's father had bilateral flexion of the fingers, a condition not otherwise defined. The patient was allergic to penicillin. The physical examination was within normal limits except for a palpable mass located at the anterolateral aspect of the right thigh. At surgery the mass was found to be covered by the fascia of the vastus intermedius muscle. It was excised.

Case No. 15

Methodist Hospital, Indianapolis
Accession No. 6933-60

This 58 year old white woman was admitted with the chief complaint of pain in the right arm which had its onset seven months previously. At its onset, the pain was of an aching and nagging character. This was followed by inability to move the right arm completely at the shoulder joint. Eight treatments applied by a chiropractor failed to afford relief. Analgesics offered by an M.D. with a presumptive
diagnosis of arthritis likewise failed to completely relieve the pain. "Electrotherapy treatments" helped a little. Approximately ten days prior to admission the patient fell backwards and experienced a sharp pain in her right arm. At this time X-ray examination revealed a pathologic fracture of the upper end of the right humerus. On questioning the patient specifically denied any severe weight loss or gain during the previous one year. A maternal uncle and a paternal aunt had had tuberculosis. The patient stated she was allergic to penicillin. Physical examination revealed normal findings except for the right upper extremity which was in a hanging cast. Marked atrophy of the shoulder muscles could be seen. After biopsy an interscapula-thoracic amputation was performed.

Case No. 16

Methodist Hospital, Indianapolis
Accession No. 6780-60

This 27 year old white male states that four months previously when an X-ray of the chest was made for an annual check-up, a bone tumor was visualized in the region of the left ninth rib. A palpable mass was present and was the only symptom elicited. A complete battery of pre-surgical laboratory tests showed normal results. At operation, a resection of the involved rib was performed.

Case No. 17

Methodist Hospital, Indianapolis
Autopsy # 106-59

A 71 year old woman was admitted with chief complaints of a feeling described as being run down, tired, and an increased need for rest along with weight loss of 12 or 13 pounds, poor appetite, and no 'pep'. Her past history included a hysterectomy 19 years previously for uterine bleeding, at which time she experienced a post operative hemorrhage. Tonsillectomy was performed prior to this because of sore throat on the left side. She had had operations on her nose on the left side and experienced tenderness or soreness in the left face over the malar region. Six or seven years prior to admission she had had a tumor removed from the left instep and was told by her doctor that it was a sarcoma and that if it were going to recur, it would do so within two years. She also fractured her left leg shortly after her hysterectomy. Two rectal operations had been performed, apparently for hemorrhoids. Physical examination revealed a number of bruised spots over her body especially on the lower extremities with definite purpura over the back and both upper and lower extremities. The blood pressure was 190/86. In addition to incisional hernias, palpation of the abdomen revealed a markedly enlarged liver with the edge at the level of the umbilicus. The liver was tender. A left upper quadrant mass was palpated and thought to be a huge spleen. A contracture of the anal canal was present. X-ray examination revealed a calcified circular mass within the spleen which was markedly enlarged. The hemoglobin was 10.3 with a 32% hematocrit; WBC was 7,300 with 66% polys and 34% small lymphocytes. A trace of albumen and 20 - 30 WBC were present in the urine which, however, concentrated to 1.022. Bone marrow studies revealed no diagnostic picture. Direct and Indirect Coombs tests were negative. The VandenBergh
Case No. 17
(Continued)

showed a .5 mg.% total, all indirect reading. The alkaline phosphatase was 2.3 Bodansky units with phosphate 3.1 mgs.% Osmotic fragility of the red cells was normal; platelets by the volumetric method were reported as .10 (normal .3-.6%). A reticulocyte count of from .1% to 1.5% was found. Following this initial admission, the patient had an incarceration of bowel in the ventral hernia, necessitating emergency surgery with repair. Approximately ten months after the first hospital admission and examination, she was again admitted. Interim history revealed a 25 pound weight loss and lethargy. Examination at this time revealed a small calcified nodule in the upper pole of the left lobe of the thyroid. The spleen was again noted to be massively enlarged, filling the left side of the abdomen and extending across the right abdomen. The liver was palpated 3 cm. below the right costal margin. A trace of pitting edema of the ankles was noted. At this time further roentgenographic study revealed osteolytic lesions in the skull. A breast tumor was found and examined following excisional biopsy revealing a benign fibroadenoma. A review of the skin lesion from the right side of the foot examined some seven years previously revealed a dermatofibroma. Extensive laboratory studies were undertaken revealing a hemoglobin of 7.0 and hematocrit of 21% with a WBC of 4,850 with 76 polys, 23 small lymphs, and 1 monocyte: Eleven nucleated red blood cells present per 100 WBC. Anisocytosis, poikilocytosis, hypochromia, and polychromasia were present on peripheral blood examination. The RBC was 2.61 million per cu. mm. The bone marrow examination revealed this time occasional abnormal cells which could not be definitely identified. Hyperplasia of both erythroid and myeloid series was noted. Megakaryocytes appeared normal. Platelets were .05 vol.% RBC indices were color - 1.0; MCH - 31; MCHC - 27; MCV - 115; Saturation 0.7; Volume 1.3. Serum potassium was 4.3 mEq.; sodium 130 mEq.; chloride 103 mEq. Co2Comb. Power 22 mEq. A splenectomy was performed. A final readmission was required two months after discharge. An autopsy was performed.

The Mayo Clinic
Accession No. C3504-61

A 29 year old man registered with the complaint of swelling in the posterior portion of the lower right thigh of 7 years duration. On physical examination there appeared to be a large tumor posterior to the lower part of the femur and encircling it. The roentgenogram was interpreted as showing a large osteochondroma. 340 grams of tissue was removed from this region on January 30, 1950 and a second operation was performed 3½ months later.
Case No. 19

Methodist Hospital, Indianapolis
Accession 5058-58

This 13 year old girl was admitted two days after experiencing a sharp pain in her right leg as she walked into a large pile of sand. Following this she was able to walk with aid and was not confined. The past history was non-informing. Admission was advised after X-ray examination of the leg. Physical examination revealed a well developed young girl with no abnormal findings except for a swelling located below the knee on the lateral aspect of the right leg. This swelling was firm to touch and tender. Biopsy of the mass was performed. Routine laboratory studies show results within normal limits.

Case No. 20

Methodist Hospital, Indianapolis
Accession No. 2530-60
2653-60

A 14 year old white girl was admitted with a chief complaint of soreness in the right shoulder of 5 months' duration and palpable tumor in the right shoulder of 2 to 3 months' duration. Sudden pain was noted when the patient fell on her shoulder approximately 1½ months prior to admission. X-rays at this time revealed a "healed fracture through a cystic lesion of the upper right humerus". Other symptoms included pain in the shoulder on motion, weakness and inability to abduct the shoulder. Approximately 6 pounds of weight loss was noted during the 5 months of her present illness. Physical examination resulted in normal findings except for the right upper extremity where a noticeable enlargement about the right shoulder was found, particularly on the anterior superior aspect of the humerus. This was due to a hard tumor which was slightly tender to palpation. Atrophy of the shoulder muscles was present. A biopsy was performed followed by open curettage and packing of the residual cavity with bone chips.