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BONE TUMORS

SECOND EDITION

General Aspects and Data on 3,987 Cases

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- Incidence, sex and age distribution, and skeletal localization
- Symptoms and physical findings
- Roentgenologic features
- Gross and microscopic pathology
- Treatment
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(Second Edition)

by

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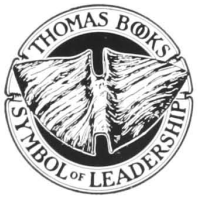

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Preface to Second Edition

THE BASIC CLASSIFICATION (modified from Lichtenstein's) employed in the first edition, with tumors comprising histologically distinctive types that have significant clinical and therapeutic implications, has stood the test of time and has gained wide acceptance. Nevertheless, some minor but useful modifications and additions have been developed and are incorporated in this volume. A few of the tumors in the earlier series have been reclassified in the light of recent knowledge.

The 9 years ending December 31, 1964, have provided more than 1,700 additional tumors, all in patients who consulted the Mayo Clinic and all studied pathologically, to augment the original series. These new cases have been incorporated into the total. The combined material has been reviewed pathologically and clinically in continuing studies in collaboration with my colleagues in the Section of Orthopedics and the Section of Diagnostic Roentgenology. It has provided significantly more follow-up information, which is critical to advancement of knowledge concerning each type of tumor. The continuing cooperation of our Section of Medical Statistics, Epidemiology, and Population Genetics has provided us with follow-up data on from 97 to 100% of the various categories of malignant bone tumor. The only group I have not studied in detail is the series of 1,044 myelomas that have been diagnosed on material obtained by aspiration of bone marrow. Patients in this group are examined and treated in the Special Hematology Laboratory, the Section of Therapeutic Radiology, and the Section of Clinical Oncology.

The new data have necessitated amplification of most of the chapters. Illustrations have been increased in order to document many of the concepts gained from study of our own material and of material sent in from elsewhere on some 1,200 problem cases in the past few years. Notable additions include comments on desmoplastic fibroma, mesenchymal chondrosarcoma, postirradiation sarcomas, and sarcomas secondary to chondromatosis and to multiple exostoses. A new chapter deals with odontogenic tumors. The bibliography for each chapter has been increased. Many of the articles that cover general aspects of diagnosis and treatment of bone tumors, and several of the more comprehensive texts available, are listed at the end of Chapter 1.

Members of the Section of Publications, the Section of Photography, and the Section of Medical Illustrations and Scientific Exhibits have made indispensable contributions to this work.

D. C. Dahlin, M.D.

Preface to First Edition

MANY OF THE MAJOR ADVANCES in present-day understanding of neoplastic and nonneoplastic diseases of bone have been made in the last two decades. In the light of current concepts, I have reviewed systematically all the bone tumors in the files of the Mayo Clinic prior to 1956. I began this review 9 years ago, and have had the help of several of my colleagues who have collaborated in the study of various facets of the over-all problem, as is indicated in the bibliography. The study has embraced more than 2,000 consecutive, unselected bone tumors. Correlation of the clinical features with the gross and microscopic features has been possible because both the case records and the gross and microscopic specimens have been available for study. Complete follow-up studies were available in almost 100% of cases largely because of the work of Dr. Henry W. Meyerding, emeritus member, Section of Orthopedic Surgery, Mayo Clinic, and emeritus professor of orthopedic surgery, Mayo Foundation, Graduate School, University of Minnesota, whose active interest in bone tumors covered a span of nearly 40 years.

Data derived from this study were first presented in the form of an exhibit at the annual meeting of the American Medical Association held in Chicago in June, 1956. Information on skeletal localization and on age and sex distribution, as well as roentgenograms, photomicrographs, and illustrative moulages of gross specimens, was included. As a result of this exhibit, a number of orthopedic surgeons, roentgenologists and pathologists asked me to make the accumulated data available for reference. This I have attempted to do in this small volume, which is an amplification of the material presented in the exhibit.

Because proper understanding of the neoplasms of bone demands correlation of their roentgenologic, gross and microscopic features, these features are liberally illustrated. Textual material has been kept to a minimum and theoretical considerations have been almost completely avoided. The bibliography has been restricted to a few of the pertinent contributions on each subject.

In the final chapter I have discussed briefly several nonneoplastic diseases of bone because they are among those that may be confused clinically and roentgenologically with neoplasms of bone. Odontogenic tumors, because of the special problems they pose, have not been included in the series.

I am indebted to Dr. David G. Pugh, of the Section of Roentgenology of the Mayo Clinic, for his review of the illustrative roentgenograms and of the comments on the roentgenologic features of bone tumors. From Dr. Einer W. Johnson, Jr., and Dr. William H. Bickel of the Section of Orthopedic Surgery, I have received invaluable aid in preparation of the comments on therapy. I am also indebted to the entire staff of the Section of Orthopedic Surgery for their co-operation in this project. To Dr. Carl M. Gambill, of the Section of Publications, and to the Section of Photography, the Section of Biometry and Medical Statistics and the Art Studio I am grateful for their contributions to this book. Dr. Arthur H. Bulbulian, of the Mayo Foundation Museum of Hygiene and Medicine, did much of the work on the original exhibit of bone tumors.

D. C. D.

Contents

BONE TUMORS

Chapter 1

Introduction and Scope of Study

THE TABULATED STATISTICS included in this book are those of an unselected series of bone tumors except for the following factors. A case was included only if a complete surgical specimen or adequate material for biopsy had been obtained. No case was included in which histologic verification of the diagnosis according to modern pathologic concepts was impossible. The pathologic features were currently reviewed in every case. The patients had all come to the Mayo Clinic for care, thus introducing a possible selection factor of questionable significance.

Accurate analysis of many of the tumors from the earlier years embraced by this study would have been impossible but for the fact that the entire gross specimen, preserved in 10% formalin solution, was available for review in practically every case. A sufficient number of new microscopic sections were made to assure that the various gross features of each lesion could be studied histologically. Such new sections were essential for the correct interpretation of certain lesions. In the average aneurysmal bone cyst, for example, the microscopic section on file was often from a nonspecific solid portion, and it was necessary to embed the curetted fragments from the specimen bottle in paraffin to obtain a preparation that reconstructed the true pathologic appearance to a degree sufficient for correct diagnosis.

Roentgenograms or the interpretation of them were correlated with the gross and histopathologic features. Although x-ray shadows do not supplant microscopic sections in final diagnosis, they frequently afford practically conclusive evidence of the malignant or benign nature of bony lesions and often indicate the histologic type. The roentgenogram may be considered part of the gross pathologic picture, delimiting as it does the part of the bone affected and, in large measure, the extent of the disease. The pathologist responsible for the diagnosis of osseous lesions handicaps himself immeasurably if he ignores their roentgenographic features. These features provide a useful guide for proper biopsy. Anyone can determine, for instance, the inadequacy of an inconclusive needle biopsy specimen or a gram of necrotic tissue excised from a tumor that gives the roentgenologic appearance of having destroyed half of a femur. A recognized limitation is that rather gross destruction, especially of cancellous bone, is necessary for a lesion to be reflected in the roentgenogram. This is well illustrated in Figures 11-13 and 11-14.

INTRODUCTION

In the case of most bone tumors the patient's local symptoms and the results of physical examination are relatively nonspecific. The usual symptoms, pain or swelling or both of these, serve mainly as a guide to the correct site for roentgenographic studies and for biopsy. Accordingly, clinical features of bone tumors have been relegated to a relatively minor place in the discussions to follow. Occasionally, however, as with osteoid osteoma that may give referred pain at a site well away from the lesion, clinical judgment is all-important.

Laboratory studies are of little aid in the diagnosis of the average bone tumor. Myeloma, with its sometimes practically pathognomonic alteration of proteins in serum or urine, is a notable exception. Alkaline phosphatase levels may be elevated in osteoid-producing neoplasms, either primary or metastatic. Elevated levels of acid phosphatase point to metastatic prostatic carcinoma. The ominous nature of rapidly growing sarcomas such as Ewing's tumor may be suggested by systemic evidences that include fever, anemia, and rapid sedimentation rate of erythrocytes.

Physiologists, chemists, and electron microscopists are attempting to clarify some of the basic problems relative to the diagnosis and nature of neoplasms, including those in bone. Some day a simpler method may be found for indicating the biologic capability of each bone tumor that presents a problem. As of now, however, the diagnosis on which therapy must be predicated and prognosis estimated depends upon correct interpretation of material removed for biopsy and stained by techniques that have been known for decades, sometimes augmented significantly by gross pathologic alterations including those reflected in the roentgenogram.

In the interest of brevity a somewhat dogmatic stand will be presented in the chapters to follow. This will be based on the study of Mayo Clinic cases and a review of the literature. When significant differences of opinion exist, these will be indicated in the text or in the bibliography.

Practical Approach to Rapid Histologic Diagnosis

Successful therapy of malignant disease depends upon the institution of treatment before systemic dissemination has occurred. It is axiomatic, therefore, that when the treatment of choice is ablative surgery it should be instituted at the earliest practicable moment in an attempt to remove the tumor before the neoplastic embolization that leads to death of the patient has occurred.

In at least 90% of bone tumors there are soft portions that can be sectioned and examined for immediate diagnosis. In most cases these soft portions afford the best material for diagnosis. For example, in sclerosing osteogenic sarcoma there are almost invariably such noncalcified zones at the periphery of the tumor. Study of the roentgenogram will guide the surgeon to these zones from which to obtain biopsy specimens for early diagnosis. Protracted decalcification of densely sclerotic portions of the tumor or adjacent cortical bone add nothing but delay in the institution of therapy.

Fresh frozen sections allow an immediate, accurate, definitive diagnosis in more than 90%

of the cases of bone tumor. There should be no problem in recognizing the rare lesion too difficult or too ossified for rapid interpretation. As with fixed sections of various types, good histologic preparations and sound basic understanding of the pathologic features are requisites for successful interpretation of fresh frozen sections. Deficiency in either requisite will tend to make one deprecate this diagnostic medium. Actually it has several advantages over conventional permanent-section techniques. First, it allows immediate appraisal of the adequacy of the specimen for biopsy. Edematous tissue around the tumor, necrotic neoplastic tissue, or benign portions of the lesion with frankly malignant foci may otherwise be considered representative of the pathologic process. Second, if the lesion proves to be of an inflammatory nature, the pathologist is guided to proper bacteriologic techniques. Finally, and most important, in the case of those malignant tumors best treated by ablative surgery, definitive therapy can be carried out immediately. Dockerty, in 1953, detailed the technique that has been employed successfully in our laboratory, with minor variations, for more than 50 years.

The pathologist who is averse to making a definitive diagnosis on fresh frozen sections should have permanent sections ready for diagnosis in 24 hours in the case of most bone tumors, provided the surgeon has procured the most suitable tissue for biopsy. Pathologists are becoming increasingly aware that they can, after examination of the roentgenograms, give the surgeon valuable counsel regarding the biopsy procedure.

Use of permanent-staining techniques other than the ordinary technique with hematoxylin and eosin are rarely necessary because they are of insignificant value in most cases. On some occasions a stain for mucus helps in the differentiation of metastatic carcinoma from primary neoplasm of bone. A stain for reticulin in examples of reticulum cell sarcoma has questionable value because atypical tumors often show equivocal amounts of stainable reticulin. Even techniques for the demonstration of alkaline phosphatase in fresh material proved of no value to me in classification, this enzyme appearing in such cells as those of a pure chondrosarcoma and the endothelial cells intermixed in typical reticulum cell sarcoma.

The procurement of material for biopsy of bone tumors by aspiration through a needle or trochar has become increasingly favored. Positive results obtained by this technique are dependable and of value, and at the Mayo Clinic its greatest usefulness has been in lesions of the vertebrae where it can supplant an extensive operation for surgical removal of tissue. The use of this technique is limited, however, since a negative result has little value in the face of clinical and roentgenologic evidence of significant disease. Also, in some tumors such as low-grade, well-differentiated chondrosarcomas, a large sample may be necessary to provide adequate evidence of malignant disease.

When decalcification is necessary a number of satisfactory techniques are available. Detailed considerations of them were published by Morris and Benton in 1956. A good principle is to avoid the dense bone that requires severe measures for decalcification if at all possible.

FIG. 1-1. Lymphoma permeating dense bone, a poor place for biopsy. Decalcification has ruined the cytologic features (×50).

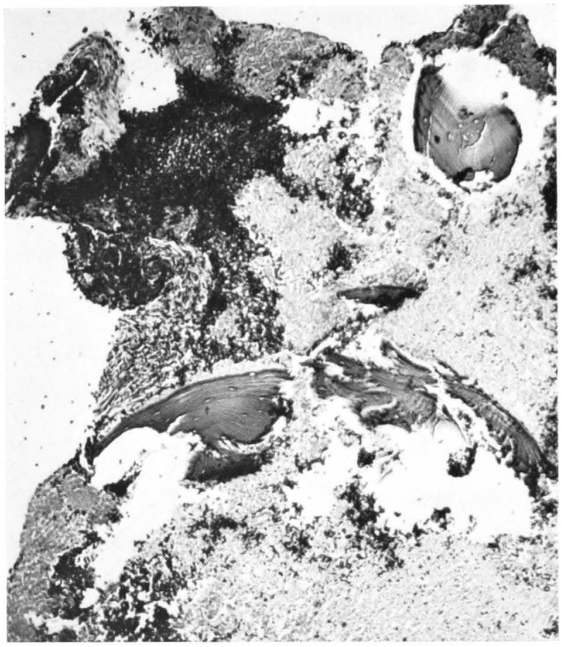

FIG. 1-2. Nondiagnostic, necrotic tissue. Frozen sections could have provided guidance to adequate tissue (×75).

Literature

Numerous articles and books concerned with bone tumors have appeared in recent years. Most authors now recognize that a useful classification must comprise entities that are pathologically distinct and have significant clinical, therapeutic, and prognostic implications. Nearly everyone has accepted the several entities that have been clarified by the works and writings of Jaffe and Lichtenstein. There are still some differences of opinion regarding exact definitions of some tumors. Accordingly, at the end of this chapter, I have provided the interested reader with a bibliography which includes the major texts that have been written in English. The list also includes many of the classic articles related to diagnostic techniques and therapy as well as some of the comprehensive studies of bone tumors in general and of those in special locations.

Classification

The classification used in this book (Table 1) is similar to that advocated by Lichtenstein. One of the significant differences is that there has been little attempt to draw a relationship between the benign and the malignant tumors because so few of the latter take origin from the former. The classification is based on the cytology or the recognizable products of the proliferating cells. In most instances, the tumors apparently arise from the type of tissue they produce, but such an assumption cannot be proved correct. For example, most chondrosarcomas begin in portions of bone that normally contain no obvious benign cartilaginous zones. In any event, basing a classification on what is actually seen histologically allows reduplication of results on subsequent

analysis. Some of the lesions in the general classification are probably not neoplasms in the strict sense.

Myxomas of the jaws are probably of odontogenic derivation. Myxomas are practically never seen elsewhere in the skeleton. Chondrosarcomas, fibrosarcomas, chondromyxoid fibromas, and portions of foci of fibrous dysplasia may have prominently myxoid features.

Hematopoietic Tumors

The hematopoietic tumors, numbering 1,481, were the most prevalent tumors of bone in the files of the Mayo Clinic. These included 1,286 cases of myeloma. Malignant lymphomas of bone, which ordinarily contain a predominance of reticulum cells and are generally referred to as reticulum cell sarcomas, contributed 195 cases. Leukemic tumor nodules in bone, while commonly found in the terminal phases of leukemia, rarely masquerade clinically as primary malignant disease of bone, although osteoarticular symptoms and signs may be prominent in acute leukemia.

Chondrogenic Tumors

The second largest group consisted of chondrogenic tumors. The tumors in this group were placed there because their histologic appearance proved or suggested a relationship to hyaline cartilage. Nearly a fourth of the total series were in this group, and the osteochondromas (osteocartilaginous exostoses) constituted nearly half of the chondrogenic group. Osteochondromas result from growth of their cartilaginous caps, making them basically chondrogenic. Chondromas, whether they be centrally or subperiosteally located, are tumors of hyaline cartilage which may show variable amounts of calcification and ossification within their substance. Benign chondroblastomas have been separated from the "wastebasket" of giant cell tumors of bone because their proliferating cells produce foci of a matrix substance quite like that of hyaline cartilage. Although chondromyxoid fibromas have a variegated histologic appearance, large or small zones ordinarily bear a striking resemblance to hyaline cartilage. Both primary and secondary chondrosarcomas are obviously related to the chondrogenic neoplasms. Mesenchymal chondrosarcoma is a distinctive subtype.

Osteogenic Tumors

In the osteogenic group of tumors the 650 sarcomas dominated the picture. For a tumor to qualify for this group the malignant neoplastic cells of the given tumor must, in at least some portions, produce recognizable osteoid substance. With this basic qualification the osteogenic sarcomas logically fall into three classes, namely osteoblastic, chondroblastic, and fibroblastic, depending upon the dominant histologic picture. The basic biologic behaviors of these three

tumor subtypes, however, are quite similar, as will be shown in the chapter devoted to osteogenic sarcoma.

The clinically indolent and pathologically slowly progressing low-grade tumors that have become generally known as parosteal or juxtacortical osteogenic sarcomas have been placed in a separate subdivision.

In the Mayo Clinic files there are 102 examples of ordinary osteoid osteoma. Without delving into the controversy as to whether this lesion represents a true neoplasm or some peculiar reaction in bone, we have arbitrarily classed it with the bone tumors. The 28 tumors that we previously called "giant osteoid osteomas" represent an unusually controversial group of cases. Lesions of this type have been called "osteogenic fibromas," "ossifying fibromas" and more recently "osteoblastomas." We employed the term "giant osteoid osteoma" because this tumor bears such a close histologic resemblance to ordinary osteoid osteoma. The prefix "giant" was meant to indicate a different biologic behavior, since tumors of this type do not share the strictly limited growth potential of the average osteoid osteoma. Benign osteoblastoma is now the generally accepted name for this tumor.

Tumors of Unknown Origin

The commonest tumor of unknown origin was Ewing's tumor, constituting 210 cases. Benign giant cell tumor, with 155 cases, was almost as prevalent. The giant cells of the benign giant cell tumor appear to arise from the stromal cells the exact origin of which is unknown. It has been suggested that they arise from undifferentiated mesenchymal cells of bone. It is impossible to substantiate the diagnosis of malignant giant cell tumor unless one can demonstrate typical zones of benign giant cell tumor in the current or previous tissue from the same case. We had only 14 bona fide malignant giant cell tumors. Adamantinoma of long bones is of unknown origin and only nine examples were present in this series.

Fibrogenic Tumors

The pathologic entity called "fibromas of bone," although quite likely not neoplastic, has been included among the bone tumors because of common usage. The files contained 50 examples. Only 100 pure fibrosarcomas of bone were encountered. It should be stressed, however, that multiple sections of all of the tumors were made, and osteoid production in any portion of a predominantly fibroblastic tumor relegated it to the osteogenic sarcoma group. The three desmoplastic fibromas encountered, although histologically benign, will be discussed in relation to fibrosarcomas.

Notochordal Tumors

This series included 122 chordomas. Although this tumor rarely metastasizes, it commonly produces death of its host by local recurrence and extension and hence it has been placed in the category of malignant tumors.

Tumors of Vascular Origin

Although the angiomatous tumors are relatively commonly manifested in roentgenograms, less that 1.5% of the histologically verified neoplasms in this series were in this group. Forty-seven of these were hemangiomas, four were hemangiopericytomas, and seven were malignant blood vascular tumors. The designation of hemangiopericytoma as benign in Table 1 is debatable.

Lipogenic Tumors

Four lipomas of bone were found. In no case did it seem possible to substantiate the unequivocal diagnosis of liposarcoma of bone. The occasional tumor with multinucleated malignant cells, possessing foamy cytoplasm and suggesting the possibility of an origin from adipose connective tissue, was classed with the osteogenic sarcomas. This decision was based on the observation that a similar histologic appearance was present in other tumors which contained zones of obvious osteogenic sarcoma.

Neurogenic Tumors

Four of the seven neurilemmomas of bone in the present series involved the mandible. No malignant neurogenic tumors originating in bone were recognized.

Unclassified Tumors

A few tumors had to be discarded from the total series because there was insufficient tissue for accurate classification. Another group, constituting approximately 1% of the total, did not fall into a niche in the classification. These neoplasms form a heterogeneous group that, for the time being, must be called "unclassified."

Skeletal and Age Distribution

Table 2 shows the skeletal distribution of the various types of tumors. It affords the reader a convenient guide for comparative incidence whether he is interested in a specific neoplasm or an affected bone. The knowledge that certain bones are practically immune to some tumors and have a marked predilection to be the site of development of other neoplasms often assists one in arriving at a correct diagnosis. It is noteworthy, for instance, that only 3 of 650 osteogenic sarcomas affected bones of the hands and wrists and that all but 1 of the 26 tumors of the sternum were malignant.

Some tumors have a decided predilection for patients in certain age groups. Knowledge of this predilection is often useful in arriving at a preoperative diagnosis. The succeeding chapters indicate, with bar graphs, the age distribution for each neoplasm. For specific figures the reader is referred to Table 3.