L. LICHTENSTEIN

BONE TUMORS

FOURTH EDITION

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With 496 illustrations in 252 figures

THE C. V. MOSBY COMPANY
Saint Louis 1972

Fourth edition

Previous editions copyrighted 1952, 1959, 1965

Printed in the United States of America

International Standard Book Number 0-8016-3094-5

Library of Congress Catalog Card Number 78-184330

Distributed in Great Britain by Henry Kimpton, London

Preface to fourth edition

Six years pass quickly, and advances in the field make it desirable once again to revise *Bone Tumors*. In doing so, I wish to express my feeling of appreciation to my readers around the world, wherever they may be, who have kept the book in active circulation for two decades. The current literature even in this limited segment of oncology continues to expand like an accordion, but the efficient services of my medical librarian, Prudence H. Hamilton, have kept my assignment from becoming onerous.

The format of the book has been preserved, but scarcely a chapter has been left unchanged. A brief new chapter on certain rare primary tumors of bone not previously considered has been introduced, dealing notably with leiomyosarcoma and malignant mesenchymoma. A fresh concept of so-called adamantinoma of the tibia, and occasionally other bones, as dermal inclusion tumors has been presented. Also, recent observations on malignant change in occasional instances of chondroblastoma, chondromyxoid fibroma, and benign osteoblastoma have been duly noted. Although the size of the text has not been appreciably increased, some 40 new illustrations, mostly roentgenograms, have been added to graphically depict new or interesting facets of many subjects, with a view to enhancing the book's usefulness. These have all been selected from my consultation material.

As always, the book remains pragmatic, and the emphasis throughout is on accurate diagnosis as an essential basis for effective treatment and realistic prognosis.

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Preface to first edition

This book is the outgrowth of a long series of studies on primary tumors of bone pursued in collaboration with Dr. Henry L. Jaffe during the period 1938-1948, while working at the Hospital for Joint Diseases in New York. These investigations were based upon the accumulated material of the hospital, richly supplemented by case material from other sources, much of it referred for consultation. As a result, certain old ideas were of necessity revised and a number of new clinical, radiologic, and pathologic concepts were advanced, which found expression in individual papers dealing with many of the benign and malignant primary bone tumors and also with a number of non-neoplastic lesions of bone sometimes mistaken for tumors. To designate some of these distinctive lesions appropriately, new names had to be coined, such as benign chondroblastoma, chondromyxoid fibroma, non-osteogenic fibroma, fibrous dysplasia, eosinophilic granuloma, and aneurysmal bone cyst, which have since gained wide acceptance.

I have been repeatedly urged by my colleagues in pathology, radiology, and orthopedic surgery, particularly, to make the individually published papers dealing with bone tumors more readily available by incorporating their subject matter into a monograph. In the course of preparation of this book, the previously published articles have all been revised and brought up to date, while certain new sections dealing with subjects not previously covered; namely, osteogenic sarcoma; tumors of vascular, fat-cell, and nerve origin; so-called adamantinoma of limb bones; carcinoma metastatic to bone; and the skeletal manifestations of tumors of hematopoietic origin, have been added to enchance its usefulness and give more complete coverage of the field. Further, since as much mischief is done by overdiagnosis as by failure to recognize malignant tumors promptly, a section has been added as an appendix, dealing with certain non-neoplastic lesions of bone which are sometimes mistaken for tumors; e.g., fibrous dysplasia, eosinophilic granuloma, aneurysmal bone cyst, and myositis ossificans, among others. With this exception, no extraneous subjects have been introduced.

Emphasis has been placed throughout the book upon accurate diagnosis as a basis for appropriate treatment, through familiarity with the distinctive features of each of the neoplasms presented. The time is long since past when it might be said with some justification that the clinical history, the x-ray picture, or the

response to treatment were more valuable than the pathologist's opinion. Inasmuch as the usefulness of some of the existing books in the field is seriously marred by pathologic inaccuracies, I have made it a special point to discuss or illustrate only cases in which I have had the opportunity personally to establish or verify the diagnosis by tissue examination. On the other hand, it is not intended to imply that the pertinent clinical data and the roentgenograms are not important in an analysis of the problem in diagnosis and therapy, although there are some pathologists naïve enough to believe that one can make sound recommendations in regard to treatment from a biopsy slide alone. In this book, illustrative roentgenograms have been freely utilized as a uniquely useful tool in determining the extent and topography of various skeletal lesions, and in judging their probable behavior on the basis of what they have done to the bone.

The relatively few blood chemical alterations that are of diagnostic importance have been considered in connection with each of the neoplasms concerned. It requires no lengthy dissertation to point out that in osteogenic sarcoma the serum alkaline phosphatase value is often elevated, that in approximately half the cases of multiple myeloma one observes hyperglobulinemia and/or hypercalcemia, that in carcinoma metastatic to the skeleton rapid demineralization may result in moderate hypercalcemia, and that in the case of prostatic carcinoma specifically, one commonly observes increased alkaline and acid phosphatase activity.

Problems in therapy have likewise been considered in relation to each of the neoplasms discussed. The emphasis throughout has been placed upon sound therapeutic indications, and beyond these, I do not feel that a competent surgeon needs to be told how to perform thorough curettement, resection, or amputation, any more than a skilled radiotherapist requires details of technique in most situations.

In the interest of clarity and conciseness, the regional treatment of bone tumors has been rejected as entailing unnecessary and confusing repetition. Further, no attempt has been made to employ considerations of embryologic development as window dressing, although a few specific allusions have been made when indicated. In the matter of bibliography, selected articles have been cited, and no attempt has been made to list all of the pertinent references. The literature pertaining to many of the bone tumors has become so voluminous, that it would be virtually impossible to catalogue it, even if it were desirable to do so.

I am indebted to Ruth Cordish and Lloyd Matlovsky for their painstaking illustrating in the matter of x-ray reproductions and photomicrographs; to Dr. Alex Griswold for his meticulous proofreading and general criticism of the text; and to my numerous colleagues and friends in pathology, radiology, and orthopedic surgery who have generously placed much of the interesting case material at my disposal. It would not have been possible to complete this book in its present form without their sustained interest and gracious cooperation.

Louis Lichtenstein

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Foreword to pathologists

It is my impression that standards in the reliable pathologic appraisal of tumors and tumorlike lesions of bone have risen perceptibly since the first edition of this book appeared. In correspondence with pathologists throughout the country seeking help with their problems in this field, I find fewer men who fail to display good insight and many more who are reasonably well informed but want moral support or encounter atypical tumors or mavericks, so to speak, for which they have no precedents in their own experience. With reference to these unusual cases, it has been my privilege to be of assistance in resolving some of the questions, and it is the accumulation and study of this valuable material that makes it possible in time to develop new concepts.

Although this is less complimentary, I feel obliged to stress once again that some pathologists still venture opinions having a bearing on treatment and prognosis (or expect me to do so) from slide interpretation alone, without fully realizing the collateral importance of the pertinent roentgenograms and of an adequate history, including the surgeon's findings. To function in this field simply as a slide reader without benefit of good clinical orientation can be disastrous at times, since the location of a lesion or what it has done to the bone (as a portent of its growth potential and probable behavior in the future) can conceivably be as significant as its cytologic picture. For example, the criteria outlined (Chapter 15) for the recognition of early chondrosarcomas apply strictly to central cartilage tumors of bone and not at all to the growing cartilage caps of osteochondromas in young patients, or to periosteal chondromas, or necessarily to extraskeletal cartilage tumors, which have a different natural history. To cite another instance in point, a lesion of myositis ossificans at the height of its activity may appear ominous enough cytologically to suggest osteogenic sarcoma, but only if one were uninformed as to the history and the location of the mass *outside* of the contiguous bone. One could go on in this vein, but suffice it to say that this is one branch of pathology in which effective medical communication is of prime importance.

Getting down to more mundane considerations, it may be in order to comment briefly on the problems of obtaining satisfactory bone sections. Altogether, I find that, while some laboratories turn out consistently good or excellent bone

sections many more leave a great deal to be desired. By and large, a pathologist gets only as good a preparation from his tissue technician as he expects, and otherwise competent technicians can be taught to improve the quality of their bone preparations. Without going into details of procedure, a few practical suggestions may be helpful. Tissue blocks should be carefully trimmed, so as to be neither too large nor more than several millimeters in thickness, and here a band saw can often be used to advantage. Whenever possible, bits of soft tissue that do not require decalcification should be processed separately, since these afford the best cellular detail. Not infrequently one has to dig them out of the bone lesion with a knife point. Fixation in Zenker's solution often yields better results than conventional formalin fixation, but this is not essential. Also, irrespective of whether one uses nitric acid or formic acid (in adequate volume) for decalcification, perhaps speeded up by an electrode device, or whether one resorts to modern chelating agents, meticulous attention must be given to the determination of the earliest point of adequate decalcification. When a bone block can be readily pierced with a pin, it is usually ready for cutting. The time required obviously varies from specimen to specimen, so that assembly-line production methods will not do. Inadequate treatment causes shattering of cement lines when the block is cut, while overdecalcification (an equally common fault) tends to obscure cellular detail. In the matter of staining, my own preference is for a deep hematoxylin (Harris) and a relatively light eosin stain.

For the rapid diagnosis of bone tumors, the frozen section approach can often be used to advantage as a guide to the choice of appropriate surgical procedure, for a quick line on prognosis and, at times, to obviate delay in amputation when this is clearly indicated. It is essential to counterstain with eosin in addition to using a nuclear stain (hematoxylin is preferred), since otherwise it is possible to overlook patches of osteoid or new bone. However, one must be wary of jumping to serious conclusions from equivocal evidence, and sometimes it is prudent to wait for paraffin sections. Pathologists whose experience in this field is limited may be reluctant to accept responsibility for a frozen section diagnosis. I do not believe that they should be expected necessarily to do so.

The value of needle biopsy of bone lesions is a controversial subject that often engenders strong feelings. This approach to diagnosis has many strong adherents in Latin America (Argentina, especially) and some in this country, mainly in institutions with very large clinic populations and relatively few hospital beds, where they have made a virtue of necessity. My own impression is that the method has only limited usefulness when applied to bone tumors specifically, in lesions in vertebral bodies (provided the operator is skilled in localization), with foci of metastatic carcinoma (where the finding of even a few cell nests affords an unequivocal diagnosis), and in some few primary tumors of strikingly uniform cytology, such as myeloma or chordoma (in which one can often obtain a representative field of diagnostic value by random sampling). In most other situations, speaking quite candidly, I dislike needle biopsy and shy away from it (if there is any alternative) in the belief that the meager cytologic picture

thus obtained is frequently not representative of the lesion as a whole, nor too informative, and may in fact be misleading as often as it is helpful. It's something like riding a bicycle with your hands tied behind your back: it's a good trick if you get away with it, but if you hit an obstacle, you're apt to fly over the handlebars and break your neck.

Louis Lichtenstein

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Chapter 1

General remarks on the clinical management of bone lesions that may be tumors*

This brief introductory chapter seems to me to be as valid today as it was when it was first written almost twenty years ago, and it has therefore been retained without change in this fourth edition. The admonition is directed mainly toward physicians and surgeons who see bone tumors only occasionally or whose experience with them is still limited.

Before launching into specific details, it seems important at the outset for overall orientation to emphasize certain basic general principles entailed in the recognition and appropriate treatment of bone lesions that may be neoplasms. (If any of these views are restated in subsequent chapters, the repetition is intentional and deemed justified by the importance of the points stressed.)

1. If a patient complains of persistent pain, swelling, or limitation of motion in an extremity or some other skeletal part, obtain good roentgenograms promptly. If these disclose a significant skeletal lesion that may be neoplastic, do not guess at its interpretation but obtain a reliable opinion. Roentgenograms are essential in determining the extent and topography of various skeletal lesions and in judging their probable behavior on the basis of what they have done to the bone. It must be recognized, however, that radiologic interpretation has its inherent limitations and that, as a rule, biopsy is required for definitive diagnosis. Despite the impression that still prevails in some quarters, there are no pat formulas for the roentgen-ray diagnosis of bone tumors, and most of the allegedly pathognomonic signs, while sometimes helpful, are often fallacious (Chapter 2).

2. The problem in diagnosis should be analyzed before surgery is undertaken since the choice of procedure, whether it be conservative biopsy, curettement, resection, or amputation, varies with circumstances. Needle biopsy, incidentally, has only limited usefulness in the diagnosis of bone lesions. The planning of an advantageous approach often calls for good liaison between surgeon,

*Lichtenstein, L.: Primary malignant tumors of bone, CA, A Bulletin of Cancer Progress 4:12, 1954.

radiologist, and pathologist. While this principle appears self-evident and is generally recognized as sound, in actual practice some men pay only lip service to it and seek advice after the fat is already in the fire, so to speak. An important corollary is that the pathologist must be more than a slide reader, if he is to function efficiently in this field, and should have the benefit of good clinical orientation before venturing an opinion as to diagnosis and/or prognosis.

3. Definitive treatment, whether by surgery or irradiation, should be predicated upon accurate pathologic diagnosis. The time is long since past when it might be said with some justification that the clinical history, the roentgenogram, or the response to treatment was more valuable than the pathologist's opinion. I am unalterably opposed to blind irradiation of skeletal lesions believed to represent tumors, except perhaps for palliation of far-advanced malignant tumors in inaccessible sites. By the same token, I am categorically opposed to radical surgery undertaken on the strength of a roentgen-ray impression alone, however well founded it may seem. What appears to be an obvious osteogenic sarcoma, for example, justifying ablation of an extremity, may conceivably prove to be a lesion of sclerosing metastatic carcinoma.

4. If roentgen therapy is the treatment of choice for whatever reason, employ the smallest dose calculated to be effective, if only because of the potential hazard of postirradiation sarcoma (after a latent interval usually of five years or more).

5. In dealing with what appears to be a malignant bone tumor, before resorting to radical surgery, obtain expert opinion if there is any reasonable doubt in regard to the diagnosis of sarcoma. Apart from any medicolegal liability entailed, it is possible that the lesion is not so serious as you think. Thus, osteomyelitis may simulate Ewing's sarcoma on occasion, as may rapidly developing lesions of eosinophilic granuloma. Instances of aneurysmal bone cyst are occasionally mistaken for aggressive giant-cell tumors and sometimes for osteogenic sarcoma. With reference to lesions held to represent osteogenic sarcoma, one must be particularly careful to make certain that the condition does not represent some other less serious lesion exhibiting active new bone formation for whatever reason, e.g., periosteal ossification, myositis ossificans (in an active stage), ossifying hematoma, or exuberant callus. In the matter of recognizing and treating skeletal lesions in general, it is my impression that more mischief is done currently through overdiagnosis than through failure to recognize malignant tumors promptly.

6. If, on the other hand, the malignant nature of a bone lesion has been clearly established, treat it without undue delay and as aggressively as may be necessary. The result of compromise and temporizing (too little and too late) is usually complete therapeutic failure. In dealing with early chondrosarcoma, for example, delay many sometimes mean the difference between cure and ultimate fatality. This urgency may apply also to instances of central fibrosarcoma and primary reticulum-cell sarcoma, which can also be cured if they are appropriately treated before metastasis has developed.

Chapter 2

General remarks on roentgenographic interpretation of skeletal lesions

Radiologists today are much more sophisticated in regard to bone tumors and tumorlike lesions than they were some twenty years ago, and this introductory section therefore does not have quite the impact that it did when it was first written. The views expressed, however, seem to me to be still valid, and the chapter, therefore, has been retained in this fourth edition without significant change. It is directed mainly toward younger radiologists (and orthopedists) whose experience with skeletal lesions is still limited.

Despite the impression that once prevailed, there are no pat formulas for the roentgen diagnosis of bone tumors, and most of the allegedly pathognomonic signs, while sometimes helpful, are often fallacious. It is true, for example, that a sclerosing tumor in the lower end of a femur, which has obviously penetrated the cortex and provoked the formation of perpendicular radiopaque striations within the cuff of tumor tissue beneath the raised periosteum, will in all probability prove to be an osteogenic sarcoma. On the other hand, if a radiologist necessarily expects this distinctive appearance as a criterion for diagnosis, he is very likely to miss more than half of all the osteogenic sarcomas that he encounters, because the indications of new bone formation and of periosteal reaction to cortical perforation by tumor are often much more subtle. In fact, there are an appreciable number of osteogenic sarcomas, mainly of osteolytic type, whose roentgen appearance is so equivocal that it is hardly possible to venture any definitive diagnosis prior to biopsy, although one may perhaps suspect the presence of a malignant neoplasm. As for the particular sign commonly alluded to, not only is this not constant, as indicated, but it is also not actually specific. That is to say, the finding of perpendicular striae of periosteal new bone is not in itself an indication necessarily of osteogenic sarcoma, inasmuch as it may be observed on occasion as a reaction to the presence of metastatic carcinoma, Ewing's sarcoma, or even tuberculosis of the shaft of a long bone.

To cite another instance in point, while it is true that an occasional lesion of

Ewing's sarcoma may manifest reactive striations of periosteal new bone laid down parallel to the cortex (so-called "onionpeel" effect), most lesions will not present this appearance. Moreover, this pattern of periosteal new bone apposition, when present, is not in itself indicative necessarily of Ewing's sarcoma, for it may be observed at times with active osteomyelitis and even in an occasional instance of osteogenic sarcoma. Actually, the presenting lesion in a case of Ewing's sarcoma that is still in an early stage of its evolution is usually reflected roentgenographically by a vaguely mottled area of rarefaction without any clearly discernible periosteal reaction, so that it may not be readily distinguishable from a focus of osteomyelitis. In a more advanced stage, when the tumor has already broken through the cortex and produced an overlying soft tissue mass, its appearance will readily suggest a malignant neoplasm, although again this picture may not be at all distinctive and at times simulates that of osteogenic sarcoma.

Continuing in the same vein, the roentgenographic picture formerly held to characterize giant-cell tumor of bone, namely, that of an expanded lesion presenting a trabeculated pattern suggesting an agglomeration of "soap bubbles," is not the picture presented by most instances of (untreated) genuine giant-cell tumor. Actually, this allegedly pathognomonic sign is distinctly misleading. Most giant-cell tumors grow too rapidly to provoke the pattern indicated. The latter is much more likely to be encountered with other lesions (e.g., hemangioma, nonosteogenic fibroma, fibrous dysplasia, enchondroma, or chondromyxoid fibroma) that grow more slowly and therefore permit the development of reactive grooves and spurs on the endosteal surface of the attenuated cortex overlying the lesion. More significant insofar as a diagnosis of giant-cell tumor is concerned are the location of the area of rarefaction in the end of the affected limb bone (especially in a patient past the age of 15 years), thinning and expansion of the cortex particularly on one side, and the absence of periosteal new-bone formation over the thinned and expanded cortex. However, as indicated elsewhere, even these features are not infallible guides to the correct diagnosis, and it is important to recognize that on occasion a chondrosarcoma (which does not display telltale calcification), a central fibrosarcoma (which has not as yet broken through the cortex), or even a solitary focus of myeloma may produce a roentgen picture not readily distinguishable, with any degree of assurance at least, from that of giant-cell tumor. It follows as an obvious corollary that one must reserve judgment as to the diagnosis in such cases until an adequate biopsy has been examined. By the same token, the wisdom of the practice of instituting radiation therapy on the strength of a roentgen impression alone, unverified by biopsy, is open to serious criticism.

Still another instance in which an oft-repeated radiologic cliché may actually render a disservice relates to the emphasis placed upon the presence of multiple punched-out defects in many bones, and particularly the calvarium, as a distinguishing hallmark of multiple myeloma. While no one will deny that some cases of far-advanced myeloma present this picture, it is essential to bear in mind that others present merely vaguely defined rarefactions in a number of bones and that still others show widespread osteoporosis without any obvious localized defects