PATHOLOGY OF SOFT TISSUE TUMORS

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PATHOLOGY OF SOFT TISSUE TUMORS

"In order to treat malignant tumors of mesenchymal origin one must first learn to recognize them." STOUT, 1964

To My Wife

preface

Soft tissues, such as muscle, fat, and fibroconnective tissue, constitute more than 50% of the human body but for some unknown reason have received little attention in the medical literature. No book has been devoted solely to the pathology of soft tissue tumors.

The clinical management of a number of soft tissue sarcomas has improved dramatically during the last 10 years as a consequence of combining surgery with irradiation and/or chemotherapy. No longer must the treatment of soft tissue sarcomas be viewed as hopeless. Because successful treatment depends upon the understanding of the natural history and proper classification of these tumors, a comprehensive textbook on their pathology is very much needed.

My objective in writing this text has been to place in the hands of those involved in the diagnosis and treatment of soft tissue tumors—pathologists, surgeons, medical oncologists, and radiation therapists—a book which embodies most of the pertinent information on the morphology, epidemiology, and prognosis of soft tissue neoplasms.

An in-depth discussion of fibrous, tendosynovial, adipose, muscle, vascular, neurogenic, extraskeletal bone, and miscellaneous tumors is presented in separate chapters. Each chapter is treated as a complete unit, from a histogenetic point of view, and begins with a classification of tumors and tumor-like lesions. Chapter 1 is a review of the history of classification and terminology of soft tissue tumors and contains a grading and staging system for primary soft tissue sarcomas. The Appendix summarizes recent trends in the therapy and differential diagnosis of soft tissue neoplasms and has 150 self-assessment questions.

Some topics are considered at greater length, perhaps, than their importance merits. However, after considering recent trends in terminology, classification,

grading, and staging of soft tissue sarcomas. I believe that a thorough discussion of the clinicopathologic aspects of certain tumors, e.g., fibrous histiocytomas, is warranted.

In reference to classification I have attempted to coordinate my own thoughts with those of others, and I have retained many of the terms advanced previously. However, a number of new concepts presented are based on observations deduced from studying thousands of soft tissue sarcomas and tumor-like conditions in clinicopathologic and experimental settings.

Although in selecting illustrative material I have tried to maintain a balance between photomicrographs and other illustrations, I have put weight on the light microscopic and differential diagnostic aspects of each tumor.

The references are arranged in chronologic order at the end of each chapter. This arrangement should facilitate easy location of pertinent works and help students follow the course of development of each topic. Review articles have been given preference over case reports, and I regret that many valuable reports could not be listed.

Whether I have accomplished my objective and readers will consider the information presented in this book worthwhile is not for me to determine. I would like to assure every reader that in presenting the facts and theories concerning soft tissue tumors I am completely aware that nobody has the eternal truth.

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New York

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S.I.H.

contents

chapter 1

History and Classification of Soft Tissue Tumors

LIKE so many other classifications in medicine, the classification of soft tissue tumors developed by fits and starts. It has been said that "in history there is no beginning." Indeed, in medicine similar ideas have often recurred, sometimes in ignorance of their previous appearances and other times as Starling said, "Every discovery, however important and apparently epoch-making, is but the natural and inevitable outcome of a vast mass of work, involving many failures, by a host of different observers."

This chapter is not an all inclusive account of the history of soft tissue tumors. The role of the historian is to present the facts *that were found* the way they were found. In my search for facts I do not claim to have followed all leads and exhausted all potential reference sources. Although my records may be incomplete, I present what I have found because I believe with E. R. Lang that "nothing gives a better perspective of the subject than an appreciation of the steps by which it has reached its present state."

THE PERIOD OF GROSS PATHOLOGY

(From Antiquity to Bichat)

The earliest description of cancer is in the *Smith Papyrus* which dates prior to 2000 B.C. and may have been written by the famous Egyptian physician Imhotep. It is regarded as the oldest nucleus of scientific medical knowledge and is in the possession of the New York Academy of Medicine (Fig. 1-1). The *Papyrus Ebers*, which is housed in the Library of Leipzig and was written in 1552 B.C., a century before the exodus of the Israelites, is a collection of therapeutic suggestions such as "Cancer is a tumor which is not to be touched" and "If the tumor goes and comes under your finger, trembling even when your hand is still, it is a fatty tumor, and treat it with the knife." The Egyptians are regarded as the founders of Medicine, but without question they included various non-neoplastic swellings in their description of tumors.

The fatalistic view of ancient physicians who believed that "cancer is incurable because it cannot be cured; if curable, it is not cancer" was also the view of Hippocrates (460–375 B.C.) who advised never to operate on an ulcerating cancer. Hippocrates contributed to the literature on soft tissue tumors by giving the first description of nasal angiofibroma.

Celsus (25 B.C.–A.D. 50) in his *De re Medicina*, which is the oldest medical document after the Hippocratic writings, attempted to separate benign neoplasms, e.g., lipoma and ganglion, from malignant growths and described the enlargement of the axillary lymph nodes in association with cancer of the breast.

The better understanding of soft tissue tumors, like that of many other tumors, was held back for centuries by, among other things, misuse and misunderstanding of various names and definitions. For example, etymologically *carcinoma* means "crab-like tumor" (Greek) for which the Latin equivalent is *cancer*; therefore, sarcomas were not regarded as cancers or malignant tumors. Galen's definition of sarcomas as "fleshy excrescence" led to the description of swellings as well as benign tumors as sarcomas or "fungus." Galen (A.D. 130–200) did not entirely neglect surgery, but he considered surgical intervention of secondary value because he believed that most diseases are constitutional and not local affections (Fig. 1-2). The doctrines of Galen were repeated for centuries and celebrated surgeons such as Albucasis of Arabia (A.D. ?–1105) advised: "Refrain from attempting to excise tumors which are of a livid color and of an irregular aspect, for these tumors are cancerous." Arderne (1306–?), celebrated English surgeon of the Hundred Years' War was equally pessimistic. He said, "I have never seen any man who

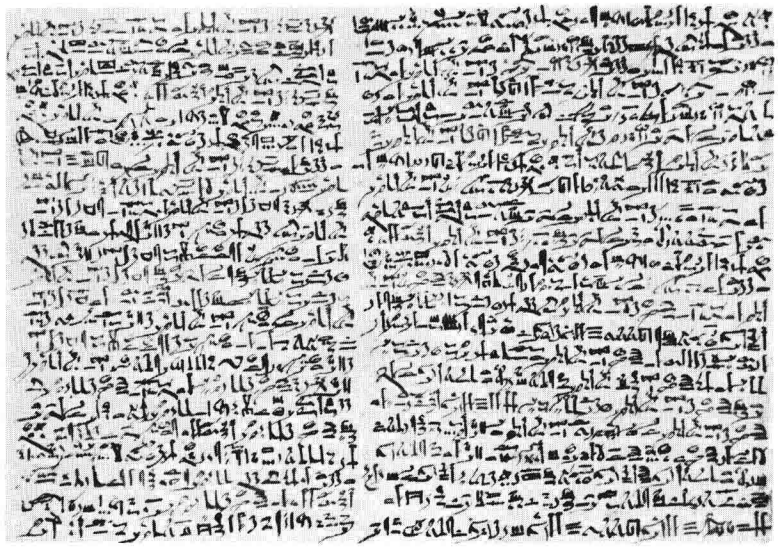

Figure 1-1. *Smith Papyrus,* 2000 B.C. (Courtesy of New York Academy of Medicine Library.)

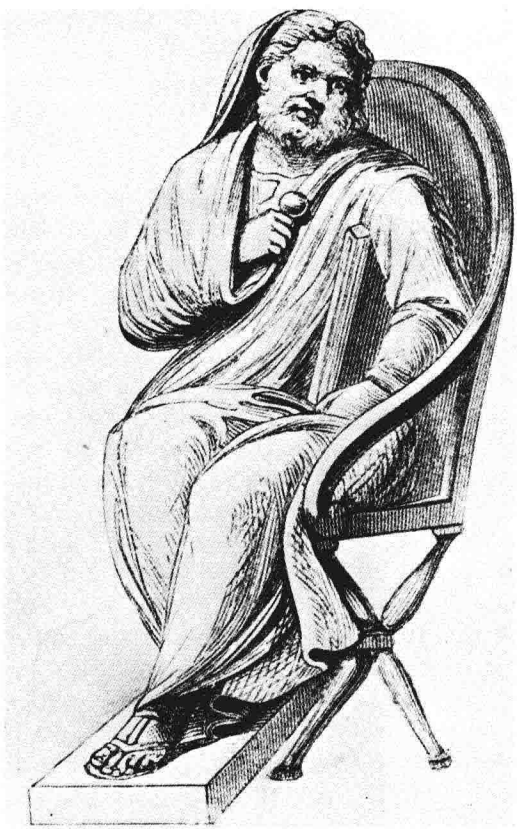

Figure 1-2. Galen (A.D. 130–200).

recovered from cancer but I have known many who died of it and it will only give you disgrace if you operate. There is no cure, and death is at the gate."

A French surgeon, the most eminent authority on surgery in the fourteenth century, Guy de Chauliac (1300–1368), was a man with different views. He believed in excising cancer at an early stage with the knife and recommended, in his book published in 1478 after his death in Lyon, cautery for the fungus (sarcoma) variety.

Soon after the invention of printing by Coster of Haarlem (1440) and Gutenberg of Mainz (1450) the first printed medical book *De Sermonum Proprietate Seu de Universo* written by Rabanus Maurus was published in Strassburg in 1467. It was followed soon by the appearance of the first printed surgical treatise, written by Brunschwig and published in Strassburg in 1497 (Fig. 1-3). From the beginning of the sixteenth century printing was fully utilized to disseminate medical information in the form of text and illustrations. The first picture of an amputation was published by Gersdorff in 1517 (Fig. 1-4).

Progress in medicine was blocked by the lack of knowledge about the composition of the human body. Vesalius (1514–1564), of Brussels, who attended the University of Louvain and Padua, wrote the

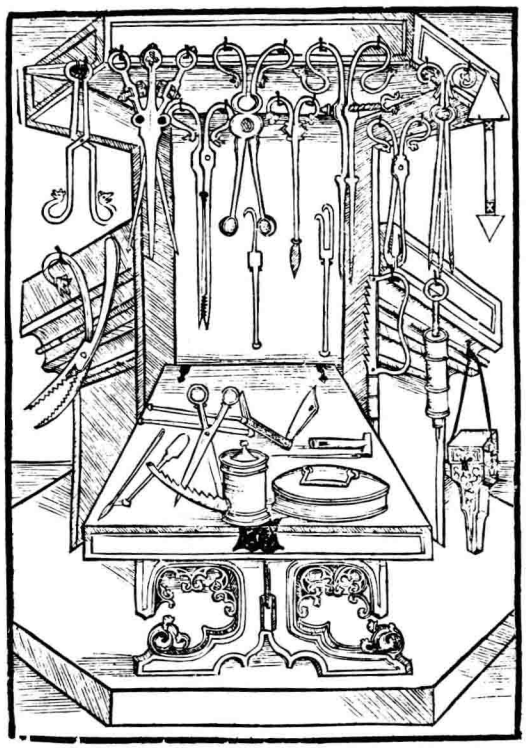

Figure 1-3. Surgical instruments of the 15th century. (From Brunschwig, H.: Dis ist das Buch der Cirurgia Hantwirkckung der Wundartzny von Hyeronimus Brunschwig. Strassburg, Gruninger, 1497.)

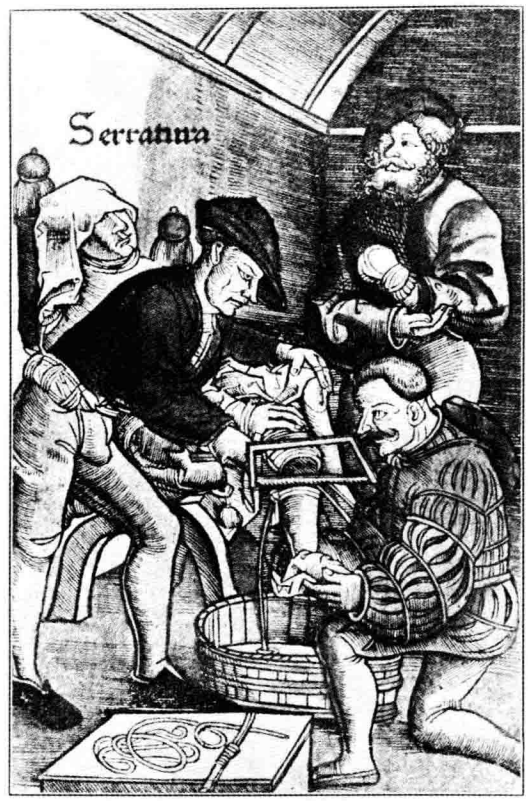

Figure 1-4. The first printed picture of an amputation (From Gersdorff, H.: *Feldtbuch der Wundartzney.* Strassburg, Schott, 1517.

first comprehensive anatomic text, *De Humani Corporis Fabrica* in 1543. The magnificently illustrated work of Vesalius was the greatest event in medical history since the work of Galen. It paved the way for physiologic and morphologic studies and laid the foundation for morbid anatomy (Fig. 1-5).

Fernel (1497–1558) in his *Medicina,* in 1542, called attention to physiology, and was the first to call the subject by that name. He also introduced the term *pathology.* His book went through several editions (Fig. 1-6). He is justly called the first pathologist. He stressed the importance of necropsies and classified diseases as (1) *simple* (when confined to a part of an organ), (2) *compound* (when affecting an entire organ), and (3) *complex* (when affecting a group of organs).

Harvey (1578–1657), one of the greatest names in experimental medicine and the father of modern embryology, published *De Motu Cordis et Sanguinis* in 1628 in which he foresaw the need for microscopic observation (Fig. 1-7). The invention of the microscope opened up a new area for observation. Velsch, in 1670, described brown fat in hibernating animals. Kircher (1602–1680), a Jesuit priest, who was probably the first to employ the microscope in investigating the cause of disease, made unbelievable observations with his primitive microscope, e.g., "every kind of plant is formed of a different and wonderful union of filaments" (Fig. 1-8). Hook (1635–1703) in England published his famous *Micrographia,* in 1665, in which the first illustration of cellular structures and the word *cell* appeared. Malpighi (1628–1694) in his *De Formatione Pulli in Ovo,* in 1673, described the red blood cells. Bartholin (1616–1680) discovered the thoracic duct and the intesti-

Figure 1-5. Portrait of Vesalius (1514–1564). (From Vesalius, A.: De humani corporis fabrica libri septem. Basileae, I. Oporini, 1543.

Figure 1-7. Title page of Harvey's *De Motu Cordis et Sanguinis.*

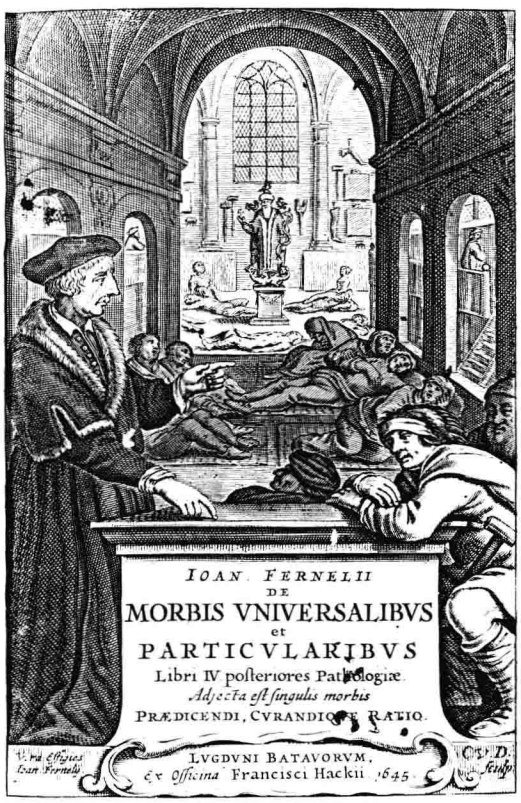

Figure 1-6. Title page of Fernel's *Morbis Universalibus.*

Figure 1-8. Athanasius Kircher (1602–1680).

nal lymphatics, and his book on this subject was published in 1653 (Fig. 1-9).

Sculteti (1595–1645), one of the greatest illustrators of surgical procedures, showed the way to remove cancerous organs. Gendron, in 1701, pleaded in a text devoted to cancers "for use of the knife rather than nostrums." Boneti, in 1700, described a tumor he called "osteoma of the mammary gland." The best illustrations of English surgery of the seventeenth century are found in the *Diary of the Rev. John Ward Extending from 1648 to 1679*, which was published in 1839 and also contained a recommendation to treat torticollis: "cut wry neck, cut three tendons."

Leeuwenhoek (1632–1723) began to publish his letters on microscopic observations in the world-renowned *Philosophical Transactions*. Among other things he is credited with the microscopic description of the striation of voluntary muscle, the sarcolemma, and epithelial cells which he scraped off the trunk of an elephant (Fig. 1-10).

The third edition of *Etmullerus'* book (Fig. 1-11A), published in 1712, contains the first published classification of tumors (Fig. 1-11B), the first reference to the use of the microscope in the diagnosis of disease (Fig. 1-11C), and a list of recommended remedies for the cure of tumors (Fig. 1-11D). Etmullerus explained the formation of tumors by saying, "If the thinner humors force their passage, while thick viscous excrements stick by the way, they gather into a body by degrees, and so cause tumours." On the other hand, his assessment of synovial lesions is fairly accurate: "Sometimes we meet with spongy swellings about the joints, that proceed from the nutritious juice of the membranes mixed with the glutinous matter that bedews the joints and are for the most part very dangerous, by reason of their tendency to cancers."

Helvetius, one of the best known therapists of the time, received 20,000 francs from Louis XIV to publish his secret remedies, including the ones for cure of cancer. They appeared in print in 1731.

Freke, in 1740, described myositis ossificans; Peyronie, in 1743, studied penile fibromatosis; Hody, in 1747, illustrated uterine leiomyoma; and Bonn, in 1763, described the synovial membrane. Despite such original observations, in 1740, de Superville stated, "It is still a dispute, whether the male or the female contributes most towards generation."

Cheselden, in 1741, in the sixth edition of his anatomy book illustrated the feasibility of scapulohumeral amputation and disarticulation (Fig. 1-12). Middletown, in 1769, published the first American contribution to medical history. He and Bard are also known for performing the first autopsy in America for the purpose of

Figure 1-9. Title page of Bartholin's *Vasa Lactea et Lymphatica*. (Courtesy of Dr. J. Rygaard.)

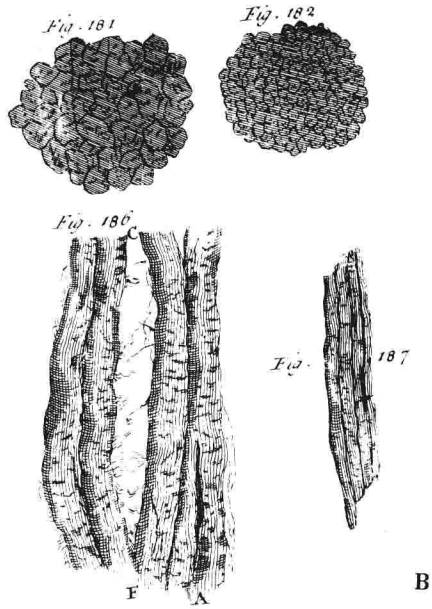

Figure 1-10. **A,** Antonj van Leeuwenhoek (1632–1723). **B,** Leeuwenhoek's illustration of striated muscle. (From Philos. Trans. London, 5:422, 1721.)

Etmullerus Abridg'd:
OR,
A Compleat Syſtem of the Theory and Practice of Phyſic.
BEING A
DESCRIPTION
OF
All Diſeaſes Incident to Men, Women and Children.
WITH
An Account of their *Cauſes*, *Symptoms*, and moſt approved Methods of *Cure*, both *PHYSICAL* and *CHIRURGICAL*.
To which is prefix'd a ſhort View of the Animal and Vital Functions; and the ſeveral Virtues and Claſſes of Medicines.
Tranſlated from the laſt Edition of the Works of *MICHAEL ETMULLERUS*, late Profeſſor of Phyſic in the Univerſity of *Lipſic*.
A BOOK very proper for Families.
The Third Edition, Corrected and much Improv'd.
LONDON:
Printed for *Andrew Bell* at the *Croſs Keys* and *Bible* in *Cornhill*, near *Stocks-Market*; and *Richard Wellington*, at the *Dolphin* and *Crown*, at the Weſt end of St. *Paul's* Church-yard. 1712.

A

The general Doctrine of Tumours being thus premis'd, we proceed to the Deſcription of particular Swellings, which we draw up in four Heads. 1. Thoſe that proceed from the Stagnation of Blood. 2. Such as are Critical. 3. Such as ariſe from the Depravation of the Lymph; and 4. Thoſe which relate to the Blood-Veſſels.

B

Having diſpatch'd the general Cure of Ulcers, we ſhall now deſcend to a few Particulars; as, 1. The Ulcers that are attended by a *Caries*, or Rottenneſs of the Bones, which muſt be particularly accounted for before the Ulcer can be cur'd. When a *Caries* begins, the Bone appears fat, oily, and yellowiſh; and when it is perfectly rotten, it becomes black, uneven, and full of little Holes. If the Bone be not expos'd to one's view, either by the naked Eye, or thro' a Microſcope, its Roughneſs and little Pits are diſcover'd by a Probe. If a *Caries* approach to the Joints, or be ſurrounded by many nervous Parts, 'tis not eaſily cur'd. How-

C

5. **Cancrous Ulcers.** Their Cauſes and Symptoms are accounted for in the Chapter of *Tumours*. As for their Cure; let the Dung of a Cat fed with River-crabs, or the Powder of a Toad and a Lizard calcin'd together in a new cloſe Veſſel, or mix'd with black Pepper, Salt, dry Soot, and Orpine, be ſprinkl'd upon the Ulcer after 'tis waſh'd with Plantain-water. If theſe prove ſucceſsleſs, apply the Oil of Mans-dung; and for the laſt Refuge Arſenic fix'd with Nitre, and mix'd with Soot and *Rulandus's* Balſam of Sulphur in the form of an Ointment; or the Oil *per deliquium* of the Arſenic thus fix'd, it being dulcify'd with Spirit of Wine. If the Cancer ſtill continue after theſe Applications, 'twill be needful to cut it off, and then burn out its Roots with a hot Iron; for if the leaſt Particle of the Ferment be left, 'twill revive again. *Alliot*

D

Figure 1-11. **A,** Title page of Etmullerus' book. **B,** Classification of tumors by Etmullerus. **C,** Recommendation to use the microscope by Etmullerus. **D,** A summary of "chemotherapy" printed in Etmullerus' book.