TUMORS of the EXTRA-ADRENAL PARAGANGLION SYSTEM (INCLUDING CHEMORECEPTORS)

ATLAS OF TUMOR PATHOLOGY

Second Series
Fascicle 9

TUMORS OF THE EXTRA-ADRENAL PARAGANGLION SYSTEM (INCLUDING CHEMORECEPTORS)

by

GEORGE G. GLENNER, M. D.
Chief, Section on Molecular Pathology
Laboratory of Experimental Pathology
National Institute of Arthritis, Metabolism, and Digestive Diseases
National Institutes of Health
Bethesda, Maryland 20014

and

PHILIP M. GRIMLEY, M. D.
Head of Ultrastructural Pathology Section
Laboratory of Pathology
National Cancer Institute
National Institutes of Health
Bethesda, Maryland 20014

Present Address
Director, Clinical Pathology Laboratories
Division of Laboratories and Research
State of New York Department of Health
Albany, New York 12201

Published by the
ARMED FORCES INSTITUTE OF PATHOLOGY
Washington, D. C.

Under the Auspices of
UNIVERSITIES ASSOCIATED FOR RESEARCH AND EDUCATION IN PATHOLOGY, INC.
Bethesda, Maryland
1974

Accepted for Publication
1973

.....

For sale by the American Registry of Pathology
Armed Forces Institute of Pathology
Washington, D. C. 20306

ATLAS OF TUMOR PATHOLOGY

Sponsored and Supported by

AMERICAN CANCER SOCIETY
NATIONAL CANCER INSTITUTE, NATIONAL INSTITUTES OF HEALTH
U. S. PUBLIC HEALTH SERVICE

and

ARMED FORCES INSTITUTE OF PATHOLOGY

EDITOR
HARLAN I. FIRMINGER, M. D.

Professor, Department of Pathology
University of Maryland School of Medicine
Baltimore, Maryland 21201
and
Scientist Associate, Universities Associated for
Research and Education in Pathology, Inc.
9650 Rockville Pike
Bethesda, Maryland 20014

EDITORIAL ADVISORY COMMITTEE

EDITOR'S NOTE

The Atlas of Tumor Pathology was originated by the Committee on Pathology of the National Academy of Sciences–National Research Council in 1947. The form of the Atlas became the brainchild of the Subcommittee on Oncology and was shepherded by a succession of editors. It was supported by a long list of agencies; many of the illustrations were made by the Medical Illustration Service of the Armed Forces Institute of Pathology; the type was set by the Government Printing Office; and the final printing was made by the press at the Armed Forces Institute of Pathology. The American Registry of Pathology purchased the fascicles from the Government Printing Office and sold them at cost, plus a small handling and shipping charge. Over a period of 20 years, 15,000 copies each of 40 fascicles were produced. They provided a system of nomenclature and set standards for histologic diagnosis which received worldwide acclaim. Private contributions by almost 600 pathologists helped to finance the compilation of an index by The Williams & Wilkins Company to complete the original Atlas.

Following the preparation of the final fascicle of the first Atlas, the National Academy of Sciences–National Research Council handed over the task of further pursuit of the project to Universities Associated for Research and Education in Pathology, Inc. Grant support for a second series was generously made available by both the National Cancer Institute and the American Cancer Society. The Armed Forces Institute of Pathology has expanded and improved its press facilities to provide for a more rapid and efficient production of the new series. A new Editor and Editorial Advisory Committee were appointed, and the solicitation and preparation of manuscripts continues.

This second series of the Atlas of Tumor Pathology is not intended as a second edition of the first Atlas and, in general, there will be variation in authorship. The basic purpose remains unchanged in providing an Atlas setting standards of diagnosis and terminology. Throughout this new series, the term chosen by the Committee on Tumor Nomenclature of the International Union Against Cancer is shown by an asterisk if it corresponds to the authors' choice, or as a synonym in bold print if it differs from the authors' heading. Hematoxylin and eosin stained sections still represent the keystone of histologic diagnosis; therefore, most of the photomicrographs will be of sections stained by this technic, and only sections prepared by other technics will be specifically designated in the legends. It is hoped that in many of the new series a broader perspective of tumors may be offered by the inclusion of special stains, histochemical illustrations, electron micrographs, data on biologic behavior, and other pertinent information for better understanding of the disease.

The format of the new series is changed in order to allow better correlation of the illustrations with the text, and a more substantial cover is provided. An index will be included in each fascicle.

It is the hope of the Editor, the Editorial Advisory Committee, and the Sponsors that these changes will be welcomed by the readers. Constructive criticisms and suggestions will be appreciated.

Harlan I. Firminger, M. D.

PREFACE

The extra-adrenal paraganglia constitute an extensive, multicentric organ system of which the function of only two components, the carotid and aortic paraganglia, are known with certainty. The morphologic similarities of paraganglia, both histologically and ultrastructurally, as well as the discovery of extra-adrenal paragangliomas secreting norepinephrine, indicate a common neural crest origin for the paraganglia and a similar, if not identical physiologic function at some stage in their genesis. These newer findings, we believe, allow an extension of the pioneering work of Raffaele Lattes which suggested the organization of paragangliomas and their tumors into distinct and definable systems despite their anatomic diversity. In this fascicle, we have attempted to present a system which organizes the paragangliomas into categories based upon an anatomic or embryologic relatedness. This emphasizes the similarities rather than the differences between such spatially separated tissues as, for example, the organ of Zuckerkandl and the carotid bodies. Tumors of these organs appear to have biologic activities of such a similar, although admittedly not identical, nature as to be of clinical significance.

The majority of extra-adrenal paragangliomas are benign and nonfunctional. The biologic activity of paragangliomas, however, cannot be predicted only on the basis of cellular morphology or pattern. It is often not possible, therefore, to determine whether an individual tumor is benign or whether it is secretory on the basis of its microscopic or histochemical (e.g., "chromaffin" or "nonchromaffin") characteristics. The presence in a patient of paroxysmal hypertension and increased excretion of catecholamine metabolites should alert the clinician to tumors not only of the adrenal medulla, but also of the extra-adrenal paraganglionic system. Clinical awareness of biologically functional interrelationships of tumors of the paraganglionic system has been rewarded in recent years by the recognition of what in the past might have been undiagnosed but treatable tumors. The classification we propose is not extended to those tissues or organs where evidence relating them to the paraganglia is uncertain and limited.

The relatively rich variety of tumors of the extra-adrenal paraganglionic system precludes the availability to any one author of sufficient examples of tumors from different sites and different biologic activity to demonstrate the morphologic variability of these tumors. In addition, the incomplete evaluation of cases of paragangliomas reported in the literature prevents obtaining reliable statistics from this source on the relative frequency and biologic activity of these tumors. We, therefore, wish to express our gratitude to the many pathologists who have sent us tissues and photographs to aid in the descriptive content of this fascicle.

George G. Glenner, M. D.
Philip M. Grimley, M. D.

ACKNOWLEDGMENTS

The photographs of gross specimens and photomicrographs, unless otherwise noted, were made in the National Institutes of Health by Mr. Robert Nye. Electron micrographs were prepared with a Hitachi HU IIE electron microscope in the Laboratory of Pathology, National Cancer Institute, National Institutes of Health with the assistance of Mr. Herman J. Michelitch.

Dr. P. H. LeCompte has kindly given us permission to use illustrations published in the first series fascicle, "Tumors of the Carotid Body and Related Structures (Chemoreceptor System)" and Dr. R. E. Coupland of Dundee, Scotland has permitted us to modify our figure 12 from his text "The Natural History of the Chromaffin Cell." The authors wish to acknowledge a debt of gratitude to Dr. A. E. Becker, Amsterdam, Netherlands; Dr. P. Böck, Vienna, Austria; Dr. B. Hamberger, Stockholm, Sweden; Dr. D. Heath, Liverpool, England; Dr. H. Ichinose, New Orleans, La.; Dr. J. E. Leestma, Chicago, Ill.; Dr. R. F. Macadam, Glasgow, Scotland; Dr. H. A. Oberman and Dr. J. R. Olson, Ann Arbor, Mich.; Dr. F. P. Probst, Umeå, Sweden; and Dr. W. C. Thacker, Greenville, Tenn. for providing us with illustrations, either published or unpublished.

We are indebted to Dr. A. J. French, Ann Arbor, Mich.; Dr. I. Costero, Mexico City, Mexico; and Dr. R. DeLellis, Boston, Mass. for providing us with microscopic specimens and clinical data, and to Dr. C. E. Martin, Pittsburgh, Pa. and Dr. M. J. Saldana, Philadelphia, Pa. for permission to include information in this fascicle from preprints of their manuscripts.

We wish to thank Mrs. Gertrude Nicholson for preparation of the diagrams, Mrs. Lee Ratner for typing the manuscript, and Miss Judith Lawson for assistance in obtaining many of the microscopic specimens depicted. In addition, the authors wish to express their gratitude to Capt. V. J. Hyams, MC, USN; Maj. H. McAllister, MC, USA; and Col. F. R. Robinson, MC, USAF of the Armed Forces Institute of Pathology for making available the microscopic specimens in their collections.

We appreciate the invaluable assistance of Dr. Harlan I. Firminger, Editor of the Atlas of Tumor Pathology, and his editorial staff.

Permission to use copyrighted illustrations has been granted by:

Almqvist & Wiksell: Stockholm

Proceedings of the 10th Nobel Symposium, Disorders of the Skull Base Region, pp. 269-272, 1968. For our figure 4A

American Cancer Society, Inc.:

Cancer 20:1473-1488, 1967. For our figures 2, 6, 17A and B, 26
Cancer 21:838-851, 1968. For our figures 20, 28, 36, 38, 39, 41
Cancer 23:1233-1238, 1969. For our figure 45
Cancer 23:1358-1367, 1969. For our figure 48
Cancer 28:692-700, 1971. For our figure 44
Cancer 28:1063-1073, 1971. For our figure 51

American Heart Association, Inc.:
Circulation 37:648-665, 1968. For our figure 7
British Medical Association: London
Thorax 25:129-140, 1970. For our figures 14, 15
Harper & Row, Publishers, Inc.—Hoeber Medical Division:
Am. J. Pathol. 24:305-321, 1948. For our figure 29
J. F. Bergmann Verlagsbuchhandlung: Munich
Arch. Klin. Exp. Ohren, Nasen, Kehlkopfheilkd. 184:214-223, 1964. For our figure I
Longman Group Limited: London
The Natural History of the Chromaffin Cell, 1965. For our figure 12
Springer-Verlag: Berlin-Heidelberg-New York
Radiologe 11:15-27, 1971. For our figures 37, 47A and B
Virchows Arch. (Pathol. Anat.) 335:356-366, 1962. For our figure 52
Z. Zellforsch. 127:220-229, 1972. For our figure 4B
University of Amsterdam: Amsterdam
The Glomera in the Region of the Heart and Great Vessels. Thesis, 1966. For our figure 10

George G. Glenner, M. D.
Philip M. Grimley, M. D.

TUMORS OF THE EXTRA-ADRENAL PARAGANGLION SYSTEM (INCLUDING CHEMORECEPTORS)

CONTENTS

ATLAS OF TUMOR PATHOLOGY

Second Series
Fascicle 9

TUMORS OF THE EXTRA-ADRENAL PARAGANGLION SYSTEM (INCLUDING CHEMORECEPTORS)

by

GEORGE G. GLENNER, M. D.
Chief, Section on Molecular Pathology
Laboratory of Experimental Pathology
National Institute of Arthritis, Metabolism, and Digestive Diseases
National Institutes of Health
Bethesda, Maryland 20014

and

PHILIP M. GRIMLEY, M. D.
Head of Ultrastructural Pathology Section
Laboratory of Pathology
National Cancer Institute
National Institutes of Health
Bethesda, Maryland 20014

Present Address
Director, Clinical Pathology Laboratories
Division of Laboratories and Research
State of New York Department of Health
Albany, New York 12201

Published by the
ARMED FORCES INSTITUTE OF PATHOLOGY
Washington, D. C.

Under the Auspices of
UNIVERSITIES ASSOCIATED FOR RESEARCH AND EDUCATION IN PATHOLOGY, INC.
Bethesda, Maryland
1974

Accepted for Publication
1973

.....

For sale by the American Registry of Pathology
Armed Forces Institute of Pathology
Washington, D. C. 20306

ATLAS OF TUMOR PATHOLOGY

Sponsored and Supported by

AMERICAN CANCER SOCIETY
NATIONAL CANCER INSTITUTE, NATIONAL INSTITUTES OF HEALTH
U. S. PUBLIC HEALTH SERVICE

and

ARMED FORCES INSTITUTE OF PATHOLOGY

EDITOR
HARLAN I. FIRMINGER, M. D.

Professor, Department of Pathology
University of Maryland School of Medicine
Baltimore, Maryland 21201
and
Scientist Associate, Universities Associated for
Research and Education in Pathology, Inc.
9650 Rockville Pike
Bethesda, Maryland 20014

EDITORIAL ADVISORY COMMITTEE

EDITOR'S NOTE

The Atlas of Tumor Pathology was originated by the Committee on Pathology of the National Academy of Sciences–National Research Council in 1947. The form of the Atlas became the brainchild of the Subcommittee on Oncology and was shepherded by a succession of editors. It was supported by a long list of agencies; many of the illustrations were made by the Medical Illustration Service of the Armed Forces Institute of Pathology; the type was set by the Government Printing Office; and the final printing was made by the press at the Armed Forces Institute of Pathology. The American Registry of Pathology purchased the fascicles from the Government Printing Office and sold them at cost, plus a small handling and shipping charge. Over a period of 20 years, 15,000 copies each of 40 fascicles were produced. They provided a system of nomenclature and set standards for histologic diagnosis which received worldwide acclaim. Private contributions by almost 600 pathologists helped to finance the compilation of an index by The Williams & Wilkins Company to complete the original Atlas.

Following the preparation of the final fascicle of the first Atlas, the National Academy of Sciences–National Research Council handed over the task of further pursuit of the project to Universities Associated for Research and Education in Pathology, Inc. Grant support for a second series was generously made available by both the National Cancer Institute and the American Cancer Society. The Armed Forces Institute of Pathology has expanded and improved its press facilities to provide for a more rapid and efficient production of the new series. A new Editor and Editorial Advisory Committee were appointed, and the solicitation and preparation of manuscripts continues.

This second series of the Atlas of Tumor Pathology is not intended as a second edition of the first Atlas and, in general, there will be variation in authorship. The basic purpose remains unchanged in providing an Atlas setting standards of diagnosis and terminology. Throughout this new series, the term chosen by the Committee on Tumor Nomenclature of the International Union Against Cancer is shown by an asterisk if it corresponds to the authors' choice, or as a synonym in bold print if it differs from the authors' heading. Hematoxylin and eosin stained sections still represent the keystone of histologic diagnosis; therefore, most of the photomicrographs will be of sections stained by this technic, and only sections prepared by other technics will be specifically designated in the legends. It is hoped that in many of the new series a broader perspective of tumors may be offered by the inclusion of special stains, histochemical illustrations, electron micrographs, data on biologic behavior, and other pertinent information for better understanding of the disease.

The format of the new series is changed in order to allow better correlation of the illustrations with the text, and a more substantial cover is provided. An index will be included in each fascicle.

It is the hope of the Editor, the Editorial Advisory Committee, and the Sponsors that these changes will be welcomed by the readers. Constructive criticisms and suggestions will be appreciated.

Harlan I. Firminger, M. D.

PREFACE

The extra-adrenal paraganglia constitute an extensive, multicentric organ system of which the function of only two components, the carotid and aortic paraganglia, are known with certainty. The morphologic similarities of paraganglia, both histologically and ultrastructurally, as well as the discovery of extra-adrenal paragangliomas secreting norepinephrine, indicate a common neural crest origin for the paraganglia and a similar, if not identical physiologic function at some stage in their genesis. These newer findings, we believe, allow an extension of the pioneering work of Raffaele Lattes which suggested the organization of paragangliomas and their tumors into distinct and definable systems despite their anatomic diversity. In this fascicle, we have attempted to present a system which organizes the paragangliomas into categories based upon an anatomic or embryologic relatedness. This emphasizes the similarities rather than the differences between such spatially separated tissues as, for example, the organ of Zuckerkandl and the carotid bodies. Tumors of these organs appear to have biologic activities of such a similar, although admittedly not identical, nature as to be of clinical significance.

The majority of extra-adrenal paragangliomas are benign and nonfunctional. The biologic activity of paragangliomas, however, cannot be predicted only on the basis of cellular morphology or pattern. It is often not possible, therefore, to determine whether an individual tumor is benign or whether it is secretory on the basis of its microscopic or histochemical (e.g., "chromaffin" or "nonchromaffin") characteristics. The presence in a patient of paroxysmal hypertension and increased excretion of catecholamine metabolites should alert the clinician to tumors not only of the adrenal medulla, but also of the extra-adrenal paraganglionic system. Clinical awareness of biologically functional interrelationships of tumors of the paraganglionic system has been rewarded in recent years by the recognition of what in the past might have been undiagnosed but treatable tumors. The classification we propose is not extended to those tissues or organs where evidence relating them to the paraganglia is uncertain and limited.

The relatively rich variety of tumors of the extra-adrenal paraganglionic system precludes the availability to any one author of sufficient examples of tumors from different sites and different biologic activity to demonstrate the morphologic variability of these tumors. In addition, the incomplete evaluation of cases of paragangliomas reported in the literature prevents obtaining reliable statistics from this source on the relative frequency and biologic activity of these tumors. We, therefore, wish to express our gratitude to the many pathologists who have sent us tissues and photographs to aid in the descriptive content of this fascicle.

George G. Glenner, M. D.
Philip M. Grimley, M. D.