Pathology of Neoplasia in Children and Adolescents

FINEGOLD

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Astrocytic Tumors in Children

Foreword

Tumors of infants and children present a substantial diagnostic challenge for surgical pathologists practicing in hospitals that do not have active pediatric oncology services. Experience gained in dealing with tumors in adult patients is of limited benefit in preparing to diagnose tumors in pediatric patients. With the exception of leukemias and lymphomas of certain types, most of the neoplasms common in adults are uncommon in infants and children and vice versa. Furthermore, the mainstream of medical literature relating to pathology of pediatric neoplasms, in large part, flows through journals different from those relating to pathology of adult neoplasms.

Pathologists, particularly those not expert in the diagnosis of neoplasms of infants and children, have long needed a definitive single reference source on the pathology of such neoplasms. This monograph, written by experts in each of the subjects covered and carefully edited by Dr. Milton Finegold, admirably fills this need.

Pathology of Neoplasia in Children and Adolescents provides a scholarly and up-to-date review of the hereditary, cytogenetic and immunodeficient mechanisms implicated in the pathogenesis of pediatric cancers as well as comprehensive coverage of recent advances in our understanding of the pathophysiology and classification of tumors of various organs. The application of adjunctive diagnostic tools, such as electron microscopy, immunocytochemistry, chromosome analysis and gene probe techniques to the surgical pathologic diagnosis of pediatric neoplasms is also included.

The diagnosis and treatment of pediatric neoplasms are complex problems requiring multidisciplinary and coordinated actions to ensure rapid and accurate diagnosis as well as initiation of prompt and appropriate therapy. This monograph will serve the surgical pathologist as an indispensable and authoritative guide to the diagnosis and classification of pediatric neoplasms. It also provides pediatricians, surgeons, oncologists and radiotherapists dealing with cancers in infants and children with the pathologic bases essential for rational selection of therapy.

JAMES L. BENNINGTON, M.D.

Preface

Despite remarkable progress in biology and medicine, cancer maintains a terrifying reputation. The insidiousness of its onset, stealth of its spread, and treachery of its adaptations to our best directed treatments haunt patient and physician alike. Cancer uses the normal machinery of cell replication for its unbridled growth, takes advantage of weakness in the host's defenses to invade, and cloaks itself in host antibodies to distract and defy pursuit, making it more sinister than the attacks of microorganisms or other natural parasites whose lives and destinies involve us somehow by accident.

In children the disease seems even more horrible. There are none of the excuses that help us to rationalize adult malignancy, such as the wages of self-abuse with tobacco, alcohol and sexual promiscuity. It cannot be regarded as an untoward consequence of earning a living in a mine, factory or shipyard, where prevention is a real possibility if only individuals and society are willing. In the young, corruption of the cell's harmonious growth and differentiation leads ultimately to the wasting and weakness that frighten and anger us.

Many were offended by the declaration of a campaign against cancer by a President (Richard M. Nixon) of the United States in 1971, perhaps because of the source and the time, or because it appeared to threaten steady scientific progress and support for other deserving projects; but, in fact, we are at war. And while this war will not end with unconditional surrender, the beachheads have been secured, the weapons are improving, and the troops are gaining in optimism. As in other wars, there have been dramatic victories led by imaginative generals like Sidney Farber, whose strategy for exploiting the vulnerability of leukemic cells in children inspired the discipline of chemotherapy. There are unsung heroes, such as the oncologist-infantrymen who face the enemy directly. They are the volunteers who have to use a deadly armamentarium that induces discomfort and pain. They are the ones who courageously confront the grief and fear of parent and child while trying to sustain hope that more powerful and better aimed weapons from laboratory proving grounds can conquer the invader.

Contributing to this battle are the intelligence and support staff; the pathologists, whose job is to identify the enemy and monitor its behavior, recognize its disguises and anticipate its movements. They also scrutinize the defenses and guard against the fifth column of complicating conditions and toxicity of therapy.

This volume in the series, *Major Problems in Pathology*, may be regarded as a manual for those intelligence operations, designed to help pathologists in the field cope with their growing responsibilities. Its international cast of contributors from many disciplines has been engaged in the struggle on many fronts for many years. They offer practical advice on the ways to examine the specimens to derive the most useful information, and they describe the latest in methods of analysis. The authors indicate the benefits of collective action in the form of multidisciplinary study groups in dealing with conditions that individually occur too infrequently to provide each combatant with enough personal experience. They present what is known of hereditary and other conditions that permit the enemy to arise in the hope of directing surveillance most effectively. They provide evaluations of the fundamental research and experimental methods that ultimately will secure the victory. They dedicate this effort to the affected children and families and to their colleagues in oncology.

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The Editor is grateful to all contributors for their efforts to make each chapter comprehensive and timely. I thank my colleagues at Baylor and Texas Children's Hospital and those in the Society for Pediatric Pathology for their suggestions and criticisms. My secretary, Virginia Bates, deserves a medal and citations are in order for the valiant editors at Saunders, led by Bob Butler, who cheerfully and competently adjusted to many logistical difficulties. Special gratitude goes to Fred Gorstein, who, as *Human Pathology* editor, inspired the Symposium on Pediatric Neoplasia from which this volume grew. An outstanding physician as well as master pathologist and dear friend, Fred knows that work can be a great balm in dark times.

MILTON J. FINEGOLD, M.D.

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HEREDITARY AND OTHER ANTECEDENT CONDITIONS OF CHILDHOOD NEOPLASIA

Michael Swift, Pamela J. Reitnauer, and Kathleen W. Rao

Splendid progress has been made within the last decade in human molecular biology, cancer virology, and chemical carcinogenesis, yet the mechanisms by which most childhood and adult cancers arise remain to be identified. An excess risk of cancer can be associated with specific single genes or chromosomal aneuploidies present at the time of conception. In other situations, genetic predisposition to cancer is suspected when there is an excess of cancer, often cell-type or site-specific, among close relatives of a cancer patient. Familial aggregation does not, by itself, imply a purely genetic mechanism. Common exposure to a carcinogen could be related to the appearance of two or more similar or identical neoplasms in members of the family, particularly if the cancers arise almost contemporaneously in persons sharing a common physical environment. When a cancer excess is observed in families of probands with a particular cancer, the challenge is to identify the genetic mechanism and the environmental interaction through which this excess cancer risk is expressed.

While our understanding of inherited differences in cancer susceptibility is incomplete, what we know has practical implications and offers insight into future directions. Presently available knowledge can be used to identify persons with increased risk of specific cancers. This leads to appropriate surveillance, more rapid and efficient diagnosis, and the opportunity for early treatment. In the longer range, understanding genetic predisposition to cancer and the gene-environment interactions responsible for specific cancers may enable us to prevent a substantial proportion of clinical cancer.

The Mendelian single-gene cancer-associated syndromes offer the most favorable opportunity to analyze the role of individual genes in cancer predisposition. One advantage is that genetically predisposed individuals can be identified by the characteristic phenotypic features of the syndrome, although not all affected individuals will express the cancers associated with the syndrome. Additionally, for some single-gene syndromes there are useful clues to the mechanism of cancer pathogenesis.

AUTOSOMAL DOMINANT CANCER-PRONE SYNDROMES

Autosomal dominant syndromes present a number of advantages in the study of cancer pathogenesis. The gene can often be traced through multigeneration families, and its expression in both the cancer and noncancer phenotypes can be observed in several members of a single family. For certain of the autosomal dominant cancer-prone syn-