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The University of Texas M. D. Anderson Cancer Center, Houston, Texas

Tumors of the Brain and Spine

Foreword by Raymond Sawaya, MD, and
W. K. Alfred Yung, MD

With 73 Illustrations and 32 Tables

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FOREWORD

It is frequently stated that progress in the management of tumors of the brain and spine has not occurred in the past 25 years. Such statements seriously underestimate and misrepresent progress in managing various central nervous system tumors, the tremendous technologic enhancements that have revolutionized the imaging of the tumors and the host organ, the multitude of surgical adjuncts such as computerized imaging guidance and functional mapping of the brain and its tracts that are routinely used in the modern neurosurgical operating room, and the highly conformal delivery of radiation to the tumor mass with remarkable sparing of the surrounding nervous tissue. Underlying these technologic improvements are the changes in philosophy that have resulted in a true multidisciplinary approach.

Equally significant is the molecular revolution that is identifying key markers behind the genesis of brain tumors, their proliferation, and their resistance to therapy. These molecular discoveries have ushered in the era of molecular targeted therapy, as first demonstrated by the extraordinary success story in chronic myelogenous leukemia of imatinib (Gleevec). The rational combination of targeted agents will revolutionize the way chemotherapy is given, either alone or in conjunction with radiotherapy.

Lastly, focused attention to patients' well-being has emphasized all measures of quality of life, has encouraged greater participation by patients and their caregivers in the decision-making process, and has encouraged the development of a variety of quality-of-life measurement tools to ensure that adverse effects of treatment are recognized and addressed.

In this monograph of the M. D. Anderson Cancer Care Series, the authors have captured the essence of the progress experienced to date and, in the most appropriate multidisciplinary fashion, they have outlined the principles behind patient assessment, decision making, and management of tumors of the brain and spine. Their expertise and commitment to their patients are evident throughout.

Raymond Sawaya, MD
W. K. Alfred Yung, MD

PREFACE

Although the annual incidence of intrinsic tumors of the central nervous system (CNS)—about 17,000 to 20,000 in the United States—is much lower than that of more common cancers arising in the lung, breast, or other sites, CNS tumors are prominent in oncology for several reasons. First, they attack the very structure of our personhood and in so doing, create fear and functional deficits as profound as they are disturbing to patients and their families alike. Second, CNS tumors can be difficult to cure when they are infiltrative or located in places that are difficult to access surgically without putting patients at some risk. Third, since tumors originating in any organ system can secondarily affect the brain or spine, much crossover exists between neuro-oncology and general oncology. And finally, CNS tumors are prominent in oncology because of the great strides being made in our understanding of these tumors on a molecular and genetic level and because treatments can now be based on hitherto unrecognized genetic alterations, advances that go hand in hand with similar knowledge being gathered in all the subspecialties of oncology.

Because of our rapidly increasing knowledge about tumors of the brain and spine, these tumors are becoming more treatable—either for palliation or for cure—than ever before. The effects of environmental exposures on tumor formation are coming more into focus, and epidemiologic knowledge is now linking nicely with molecular genetic alterations derived from kindreds susceptible to brain tumor formation. Such alterations have been correlated with a progression from benign to malignant forms of several tumor types, most notably the astrocytoma; and although an initiating genetic mutation cannot yet be traced for most tumors, molecular genetics is now being used in neuropathologic diagnoses to supplement more traditional histologic approaches. Diagnostic tools such as magnetic resonance imaging continue to develop and have become quite sensitive, albeit less than perfectly specific, in revealing CNS tumors at earlier and earlier stages. Surgical procedures too are advancing through a combination of more complex technologies and the development of a cadre of neurosurgeons specialized in the nuances of tumor care.

In the new world of CNS oncology, maximally complete resection is followed by conformal radiotherapy and often by chemotherapy, the selection of which is based on the tumor's susceptibility to drugs that have biological actions known to interact with the tumor's particular

molecular signature. For example, oral temozolomide is better tolerated by patients than predecessor intravenous chemotherapeutic agents and is more effective in patients with epigenetic silencing of the *MGMT* gene associated with DNA repair. This agent has become the standard of care for patients with anaplastic or malignant astrocytomas after resection and irradiation. In the future, we may find that today's groundwork in immunotherapy or in stem cell biology will further improve our therapeutic reach.

The chapters of this book collectively weave a tapestry that depicts the broad range of medical, surgical, and radiotherapeutic approaches to neuro-oncology as it is practiced at M. D. Anderson Cancer Center, along with the diversity of disciplines needed for effective therapy. This is now the sixth book in the M. D. Anderson Cancer Care Series. The first of these was published in 2001 and was devoted to breast cancer. This book, like the others, highlights integrated care and focuses on treating the patient through the entire spectrum of a disease.

We thank Walter Pagel for shepherding the Cancer Care Series since its inception and Elizabeth Hess, Manuel Gonzales, and Tamara Locke of the Department of Scientific Publications for their dedication to producing this book. And we thank you, the reader, for your interest in this most intricate and fascinating corner of oncology in which we practice our art and our science.

Franco DeMonte, MD
Mark R. Gilbert, MD
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