CHAPTER 1

Introduction

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Introduction

Cancers of the central nervous system (CNS) are considered to be among the most devastating of all cancers. The brain and spinal cord are complex organs that control the CNS, the peripheral nervous system, and many of the voluntary and involuntary systems of the body. The effects can be devastating for the patient and the family when cancer attacks the CNS. It has been found that 20%–40% of all cancers metastasize to the brain (Cairncross, Kim, & Posner, 1980; Gavrilovic & Posner, 2005; Nathoo, Chahlavi, Barnett, & Toms, 2005; Posner, 1992).

Many families have experienced the effects of a CNS cancer. The diagnosis and death of Senator Edward Kennedy in 2009 brought public awareness to this disease state. All patients will have some change in personality, memory, motor skills, or executive functioning during the illness trajectory that compromises their quality of life. Care of those living with a brain and spinal tumor requires a broad knowledge base in neuro-oncology and a sensitive and realistic approach that optimizes quality of life and permits a sense of hopefulness to prevail. Care of informal caregivers also is an area of ongoing study.

Historical Perspective

The brain being the domicile for all the mysteries of the body has been suspected for ages. Dating back to the middle Stone Age period, archeologists found skulls with holes bored into them, a procedure called trepanation. The healed holes reveal that the surgeries had been successful and the patients had survived. Trepanation was carried out until the beginning of the 20th century. This treatment was believed to permit evil spirits to be removed and to treat seizures, headaches, and blindness. The first experiential physiologists, Galen, Vesalius, and Willis, whose work dated back to 130–200 AD, described on parchment paper the anatomy of the brain. Galen's view of human anatomy dominated European medicine for 1,500 years (Kaye & Laws, 1995).

Modern brain surgery was first reported by Rickman Godlee in 1884. He operated on a 25-year-old Scottish farmer who suffered from epilepsy and progressive hemiparesis. He was found to have an oligodendroglioma and subsequently died from an infection (Kaye & Laws, 1995). The discoveries in the 19th century of asepsis, anesthesia, and neurologic localization of the brain tumor allowed modern brain surgery to flourish. The 20th century found a surge of technologic advances mostly focused on diagnostic and surgical techniques. Treatment choices have remained few with no grand slams, but the discovery of temozolomide provided hope.

The 21st century has just begun to reveal advances. Personalized treatments based on tumor typing may be on the horizon. MGMT (chemically known as O-6-methylguanine DNA methyltransferase) status of the tumor was found to differentiate those patients who may be more receptive to temozolomide (Hegi et al., 2005) (see Chapters 5 and 8 for discussions regarding MGMT). Scientists are working to find the genomic makeup of tumors and to work on effective treatments to possibly cure them. Thus far, CNS cancer death rates have not declined. Oncology nurses are also more sensitive to the overall psychosocial needs of patients and family caregivers.

Epidemiology

Low-grade (grade 2) tumors, including low-grade oligodendrogliomas, astrocytomas, and mixed oligoastrocytomas, have been found over time to progress to grade 3 or 4 tumors. The time may vary depending on the genetic makeup of the tumor, which can only be determined if a surgical pathology specimen is obtained and analyzed (Whittle, 2004). Despite the surgical and oncologic advances in technology, the prognosis remains poor for high-grade tumors. The diagnosis of

CNS cancer, with the daunting statistics on median survival of patients with high-grade tumors being less than 12 months, leaves little hope for the patient. Current knowledge reveals that most low-grade tumors will progress to high-grade tumors (van den Bent et al., 2005).

The National Cancer Institute (NCI, n.d.) estimated that 22,070 new cases of brain and other CNS cancers would be diagnosed in the United States in 2009. The American Brain Tumor Association (ABTA, 2010) clarifies this statistic further by estimating that 62,930 new cases of primary brain tumors would be diagnosed in 2010. Of this total, 23,720 are malignant and 39,210 are nonmalignant (ABTA, 2010). The death toll from cancers of the CNS is estimated to reach approximately 13,000 (NCI, n.d.).

An estimated 12,920 deaths were attributed to primary CNS cancers in 2009 (Central Brain Tumor Registry of the United States, 2010). The incidence of CNS tumors is highest in developed, industrialized countries where approximately 6–11 new cases are diagnosed annually per 100,000 population; mortality rates for all types of primary CNS tumors are 3–7 per 100,000 (Feraly, Bray, Pisani, & Parkin, 2000; Parkin, Whelan, Feraly, Teppo, & Thomas, 2002). Gliomas comprise 70% of all brain tumors with the most common type, glioblastoma multiforme, also being the most lethal (Ohgaki, 2009). From 2003 to 2007, the median age of patients at the time of a brain cancer diagnosis was 56 years old (NCI Surveillance, Epidemiology, and End Results, 2009).

Some controversy exists regarding a possible increase in the incidence of brain tumors, particularly in older adults. This may be due to improvements in neuroimaging access and technology (Christensen, Kosteljanetz, & Johansen, 2003; Legler et al., 1999). Population-based incidence data from the Netherlands Cancer Registry showed a stable incidence of adult and childhood gliomas (Houben et al., 2006). In this study, an increase in incidence of high-grade astrocytomas in adults was balanced by a decrease in low-grade astrocytomas.

Although the exact incidence of metastatic brain tumors is unknown, estimates range from double to 10 times the number of primary brain tumors, with at least 20%–40% of patients with cancer developing brain metastases at some point in their disease (Cairncross et al., 1980; Gavrilovic & Posner, 2005; Nathoo et al., 2004; Posner, 1992).

Risk Factors

Little consensus exists regarding the risk factors for developing primary brain tumors. The general principles of tumorigenesis implicate an accumulation of inherited and acquired genetic alterations that allow cells to evade normal regulatory mechanisms and divide abnormally. The relationship between chromosome instability and cancer susceptibility is well established, as is the association of defective DNA repair mechanisms in individuals harboring chromosomal alterations (Busch, 1994; Wei et al., 1996). Heritable factors are implicated in a few rare autosomal dominant tumor syndromes (only one mutant gene is required to express the disease), including Li-Fraumeni syndrome, neurofibromatosis types 1 and 2, and Turcot syndrome (Ohgaki, 2009).

Environmental factors associated with this malignant transformation have been difficult to positively identify. Exposure to ionizing radiation has been established as a risk factor for CNS tumors through studies on atomic bomb survivors, as well as children treated with radiation for tinea capitis (ringworm of the scalp) (Hodges, Smith, Garrett, & Tate, 1992; Preston et al., 2002; Socié et al., 2000).

The observation that brain tumor incidence is increased in certain occupations, including firefighters, physicians, farmers, embalmers, and pathologists, has prompted studies of the effects of industrial and occupational chemical exposure, but no definitive causative agent has been found (Mazumdar et al., 2008). Studies on diet, alcohol consumption, tobacco, electromagnetic fields, and cell phone use have similarly resulted in conflicting and inconclusive findings about risk factors (Parascandola, 2001). Some viruses have been implicated in brain tumor development in animal models, but only HIV has been causally linked to brain cancer in humans (Brittain, 2002; McLaughlin-Drubin & Munger, 2008).

Clinical Practice Implications

The brain tumor diagnosis continues to provoke fear and anxiety in patients. Because of the brief median overall survival of less than 12 months for patients with glioblastoma multiforme, specialists in neuro-oncology have systematically researched the natural history of brain tumors. Through the tireless effort of those committed to improve outcomes, advances have been made in the initial surgical management of brain tumors, with a reduction in the morbidity while achieving the surgical objectives. For decades, radiation therapy has been shown to be an effective postsurgical adjuvant therapy, and the current fractionated regimen maximizes the efficacy while minimizing the toxicity of this therapy. Only recently have definitive results shown a benefit from chemotherapy drugs, particularly alkylating agents (Hegi et al., 2005).

With these therapeutic advances, the median survival today has increased several months compared to earlier last century. This is thought to be a result of both the aggressive and resistant biology of brain tumors and the difficulty with which promising agents can be delivered to the brain. To circumvent these barriers, innovations in the form of surgical bed polymer-based therapeutics delivery and positive-pressure interstitial therapy delivery have been tested in the surgical arena. Although the polymer-based therapeutics delivery methods, such as chemotherapy-impregnated wafers, have shown modest activity (Lassman & Holland, 2005), trials investigating the

utility of positive-pressure interstitial therapy delivery used to deliver chemotherapeutic agents directly into the tumor have not yet yielded positive results (Debinski, 2002).

Scientists have embraced the challenge of advancing care by dissecting the molecular biologic basis of brain tumor formation and the molecular signatures that dictate tumors' behavior. By identifying unique molecules that appear to play important roles in brain tumor biology, the field of neuro-oncology has moved forward with a tailored approach to targeting and modifying treatment. Through these efforts, the U.S. Food and Drug Administration has approved promising new agents for use against brain tumors, with the most recent approval for bevacizumab, which targets the activity of vascular endothelial growth factor. Interestingly, as the fight against these tumors advances, the use of newer agents has rewritten what is known about the radiographic changes that occur when treating brain tumors, necessitating reevaluation of previous knowledge.

Summary

Today, tools and methods to analyze tumors and their behavior are becoming more prevalent. Clearly, efforts over the past century have yielded real advances; however, we have also come to realize that gains in survival must be balanced with the maintenance of quality of life. Recognizing that what is more important to patients is the length of their good quality of life, more and more researchers have incorporated measures into clinical trials that follow quality of life. Although we have yet to cure brain tumors, clear steps forward have been taken toward reaching this ultimate goal. Each advance injects hope to the team of caregivers and, more importantly, to those who live with this diagnosis.

This book will explore the current treatment for cancers of the CNS. Nurses are trying to make a difference in the outcomes of our patients in survival and quality of life. Our future endeavors will focus on not only basic science questions but also on quality of life for patients, caregivers, and families.

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