A diagnosis of a malignant brain tumor is devastating to patients and their families. The patients’ inevitable loss of independence, which can occur suddenly or gradually, is tragic, and the eventual complete dependence can be overwhelming to the family and caregivers. Glioblastoma multiforme (GBM) is the most common type of primary malignant brain tumor in adults and is associated with a disproportionately high mortality rate. The highly malignant tumor grows rapidly and has a tendency to recur through treatment. The brain itself presents a multitude of barriers to treatment, such as tumor location, accessibility for surgery, and the blood-brain barrier’s natural protection. Despite access to optimal multimodality treatment, patients diagnosed with GBM have a low survival rate. Patients and families need emotional and practical support throughout the continuum of this devastating disease. Astute neurologic assessment skills and immediate and appropriate interventions are required to maintain the patient’s functional status. This article provides an overview of the treatment of GBM and reviews how oncology nurses can intervene to positively improve the quality of life of patients and their families.
or weeks. Patients who have rapidly growing tumors often present with signs of increased intracranial pressure (e.g., headache), usually accompanied by nausea and vomiting, seizures, and focal neurologic deficits such as hemiparesis, aphasia, cranial nerve dysfunction, ataxic gait, sensory loss, or hemianopsia (i.e., blindness in half of the visual field in one or both eyes) (Nolan & Gavrilovic, 2010). Gadolinium-enhanced magnetic resonance imaging (MRI) is the standard imaging procedure to diagnose and monitor GBMs (see Figure 1). MRI is significantly more sensitive than computed tomography to the presence of tumor and peritumoral edema (Earnest, Baker, Kispert, & Laws, 1985). GBM often extends microscopically, beyond the visible margins of signal-intensity abnormality on MRIs. In addition, after surgery, differentiating between recurrent tumor and scar tissue on the basis of MRI findings alone may be difficult; therefore, adding perfusion imaging, spectroscopy, or positron-emission tomography scanning may be helpful (Lobera, 2009). Computed tomography scans are used for those who cannot undergo MRI, such as patients with a pacemaker.

### Primary Treatment

Surgery is the first line of treatment for GBM. Ideally, a patient will undergo gross total resection of the tumor, but tumor location and proximity to vital structures can affect the extent of the resection. Gross total resection is the absence of contrast-enhancing tumor seen on the postoperative scan. Because of the microscopic infiltrative growth of GBM into the surrounding healthy brain, complete resection is difficult. Modern advances in surgical technologies are used, such as MRI-guided surgery, intraoperative mapping, and fluorescence-guided surgery, to optimize tumor resection. If resection is not possible, a biopsy is needed to determine definitive diagnosis because histologic tumor grade and pathology are needed when formulating the treatment plan. Some surgeons may place wafers impregnated with carmustine (an alkylating chemotherapy agent), along the resection cavity. The biodegradable wafers (Gliadel®, Eisai Inc.) release over time to target residual tumor cells. The use of these wafers may make postoperative MRI interpretation difficult and also may exclude patient participation in some clinical trials.

Standard treatment following resection or biopsy is radiation therapy concurrent with temozolomide chemotherapy (National Comprehensive Cancer Network [NCCN], 2010). Although researchers are examining varying fractionation and dosing schedules, standard radiation is 60 Gy to the tumor bed and surrounding margins given daily, five days a week (Monday through Friday) for about six weeks (NCCN, 2010). Oral temozolomide chemotherapy (75 mg/m² per day) is given seven days a week during the six-week course of radiation (NCCN, 2010). An IV preparation of temozolomide now is available commercially for patients who cannot swallow capsules. After radiation is completed, patients are given a three-to-four-week treatment pause prior to starting adjuvant therapy. Adjuvant temozolomide therapy (150–200 mg/m² per day for five days) continues monthly for a minimum of six months following the completion of radiation, provided no tumor progression is observed.

The combined modality approach became the standard of care after Stupp et al. (2005) reported the results of a large randomized phase III study conducted by the European Organisation for Research and Treatment of Cancer and the National Cancer Institute of Canada. Almost 600 patients newly diagnosed with GBM were randomized to radiotherapy alone or to radiotherapy with concurrent temozolomide followed with six months of adjuvant temozolomide as described earlier. Results demonstrated a considerable survival advantage for patients who were treated with the combined approach; median survival was 14.6 months versus 12.1 months (p < 0.001). Two-year survival also was significantly greater among patients who received combined treatment (27% versus 10%) (Stupp et al., 2005). Despite combined modality chemoradiation, adjuvant temozolomide, and optimal resection, almost 100% of patients recur (Mayer & Sminia, 2008).

### Treatment of Recurrent Disease

Repeated resection for recurrent disease is an option for a small group of patients, depending on tumor location and the risk of neurologic compromise. Additional radiation may be possible for some patients, but the tolerance of healthy brain tissue to radiation is limited because of increased risk of radiation necrosis. Total cumulative dose and interval since radiation must be considered (Mayer & Sminia, 2008). A wide variety of radiation techniques, including brachytherapy, gamma knife, and stereotactic radiosurgery, may be used for the treatment of recurrent disease.

Chemotherapy for recurrent GBM remains challenging; drug options are limited because most agents cannot cross the blood-brain barrier, which is a tightly woven mesh of endothelial cells, astrocytes, and transmembrane proteins lining the vessels of the central nervous system. The barrier restricts diffusion of bacteria and other large or water-soluble molecules from the bloodstream into the brain and provides a neuroprotective mechanism from infection and other toxins. As a result, most chemotherapy agents cannot penetrate the brain. Strategies to bypass or alter the blood-brain barrier with drugs and nanotechnology are ongoing (Caruso et al., 2010). Chemotherapy drugs for recurrent disease also may include other liposoluble alkylating agents such as carboplatin and the nitrosoureas carmustine and lomustine. Combination therapy with procarbazine,

### Table 1. Grading and Classification of Gliomas

<table>
<thead>
<tr>
<th>CLASSIFICATION</th>
<th>HISTOLOGIC SUBTYPE</th>
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</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>Pilocytic astrocytoma</td>
</tr>
<tr>
<td>Grade II</td>
<td>Astrocytoma, Oligodendroglioma; Mixed oligodendroglioma-astrocytoma</td>
</tr>
<tr>
<td>Grade III</td>
<td>Anaplastic astrocytoma, Anaplastic oligodendroglioma, Anaplastic mixed</td>
</tr>
<tr>
<td>Grade IV</td>
<td>Glioblastoma</td>
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*Note. Based on information from Louis et al., 2007.*
lomustine, and vincristine may be used, as well as other cytotoxic agents. Temozolomide and other alkylating chemotherapy agents exert their cytotoxic effect by damaging DNA, triggering apoptosis and cell death. Some tumor cells have the ability to repair that DNA damage by upregulating or overexpressing the enzyme methylguanine methyltransferase (MGMT). Methylation of MGMT weakens the ability to repair the DNA damage caused by alkylating agents (Newton, 2008) and has been shown to be an independently favorable prognostic factor (Chinot et al., 2007; Crinière et al., 2007; Hegi et al., 2005). MGMT methylation status is determined by pathologic review. Clinical trials modulating chemotherapy dosing schedules (e.g., metronomic, continuous, or frequent treatment with low chemotherapy doses and dose-dense regimens) are under way, attempting to alter MGMT methylation. Continuous exposure of a tumor cell to alkylating agents may exhaust the cells’ MGMT and improve chemotherapy effectiveness (Lee, Thatcher, Crowther, & Margison, 1994).

In 2009, bevacizumab was approved by the U.S. Food and Drug Administration for use in patients with recurrent GBM. A humanized monoclonal antibody, bevacizumab targets vascular endothelial growth factor and inhibits angiogenesis. Bevacizumab may normalize the vasculature of tumors and facilitate chemotherapy delivery, or may work by inhibiting formation of new vessels, depriving the tumor of blood supply and nutrients (Chamberlain, 2009). Antiangiogenic drugs may be synergistic with radiotherapy and decrease peritumoral edema, ultimately allowing corticosteroids to be decreased (Wen & Kesari, 2008). Some antiangiogenic drugs and molecular targeted therapy, particularly tyrosine kinase and other cell-signaling pathway inhibitors, are in clinical trials alone and in combination with cytotoxic chemotherapy (Van Meir et al., 2010). As more is understood about common molecular changes and genetic mutations found in GBM, therapy will become more individualized based on patients’ tumor genotype. Patient participation in clinical trials with these agents is encouraged to expand treatment options. Overall, the goal of any treatment for GBM should be maintaining patients’ functional status and quality of life (QOL) because cure rarely is attained. Oncology nurses should be realistic and hopeful when discussing treatment decisions and goals.

**Nursing Management and Supportive Care**

Patients with GBM are vulnerable to gradual and acute symptoms or complications related to the tumor and side effects from treatment and medications. Supportive care for commonly occurring complications such as peritumoral edema, seizure, and venous thromboembolic events (VTEs), as well as treatment-related side effects, is an integral part of neuro-oncology nursing practice. Oncology nurses usually are the most accessible members of the healthcare team and have frequent interaction with their patients, so they become the cornerstone of the healthcare team. Frequent discussions may increase trust and help to dissipate anxiety and fear. Ongoing assessment and discussion with the patient and family provide a strong foundation for early intervention and maintenance of QOL.

**Peritumoral Edema and Corticosteroids**

Peritumoral vasogenic edema occurs when plasma proteins and other water-soluble substances leak within the tumor and the surrounding brain tissue. This happens as the tumor grows and secretes vascular endothelial growth factor, developing new blood vessels that lack a normal blood-brain barrier (Batchelor & Byrne, 2006). Symptoms of increased intracranial pressure, such as headache, often accompanied by nausea and vomiting, and focal neurologic symptoms, can be caused by peritumoral edema. Corticosteroids such as dexamethasone are used to decrease edema and may produce their effect by decreasing the permeability of capillaries within the tumor. Patients are likely to be on corticosteroids multiple times throughout their disease course, such as at initial diagnosis, postoperatively, during radiation, and at tumor progression. A loading dose usually is given, followed by a divided daily dose. To reduce side effects, the lowest effective dose is prescribed and slowly tapered off as tolerable. Corticosteroids generally are associated with a large number of side effects, including gastric upset, increased risk of infection, muscle myopathy, diabetes mellitus, and mood alterations such as irritability and insomnia. Patients should be instructed to take steroids with food to decrease gastric irritation and most patients are prescribed histamine blockers or proton pump inhibitors.

Steroids can suppress immune system function, which places patients at increased risk of infection. Patients are vulnerable to opportunistic fungal infections, such as *Pneumocystis carinii* pneumonia (also known as *Pneumocystis jiroveci*). The symptoms can be nonspecific and subtle, often presenting as low-grade fever, malaise, weight loss, and cough; dyspnea and desaturation on exertion also may be present. Medication for *Pneumocystis carinii* prophylaxis commonly is prescribed, including oral sulfamethoxazole-trimethoprim, dapsone, atovaquone, or pentamidine.
Thrust, another opportunistic fungal infection, may occur in patients receiving corticosteroid therapy. Nurses should perform regular oral cavity inspections for evidence of thrust. Patients should be educated regarding symptoms of thrust and the importance of adherence to an oral care regimen. If thrust is present, treatment with antifungal agents such as nystatin oral suspension or fluconazole may be prescribed. Early identification and treatment of thrust are essential to decrease pain, prevent changes in taste and oral intake, and improve QOL.

Steroid myopathy is a common complication associated with a prolonged course of steroids. Muscle wasting and proximal weakness of the quadriceps and the triceps muscles may occur. Activities of daily living, such as standing up and ascending stairs, can be difficult and patients may require assistance. For patients experiencing mobility challenges, a multidisciplinary approach including physical and occupational therapy may be beneficial.

Steroid use is associated with sodium and water retention and can contribute to weight gain and peripheral edema; therefore, weight must be measured and fluid and electrolyte status must be monitored routinely. A low-sodium diet may be beneficial. Hyperglycemia and steroid-induced diabetes also are concerns; patients should be educated about the potential for and symptoms of hyperglycemia. Close monitoring of blood glucose levels may be warranted, and education regarding oral antihyperglycemic agents or insulin administration should occur as indicated.

Seizure Management

Seizures are the presenting symptom in 20%-40% of patients with brain tumors, and an additional 20%-45% develop seizures during the course of their illness (Batchelor & Byrne, 2006). The tumor location plays a crucial role in determining the risk of seizures (Smith, 2010), with tumors in the parietal, frontal, and temporal lobes typically producing the most seizures (Kargiotis, Markoula, & Kyritsis, 2011). Patients with temporal lobe tumors typically present with complex partial seizures frequently preceded by an aura, which is a distinctive feeling, premonition, or warning signal such as a sound, smell, or visual effect that may precede a seizure. Occipital lobe tumors may cause visual hallucinations, whereas focal sensory seizures may be seen in patients with parietal tumors (Sperling & Ko, 2006). When tumors are located in the motor cortex, unilateral focal motor symptoms usually occur (Sperling & Ko, 2006). Nurses need to educate patients and their families about acute seizure management to prioritize patient safety. Information and accurate documentation of the seizure, including type, duration, progression, and presence or lack of aura, can be helpful to optimize seizure management. Many antiepileptic drugs (AEDs) are used to prevent and treat seizures, and therapy needs to be individualized for patient tolerance and seizure control. Side effects from AEDs include somnolence, fatigue, insomnia, blurred vision, rash, elevated liver enzymes, nausea, and anorexia. Mood alterations (e.g., depression, irritability, nervousness) also may occur. Phenytoin, carbamazepine, and phenobarbital are enzyme-inducing antiepileptic drugs (EIAEDs) and have the ability to stimulate the cytochrome p450 enzyme system, altering the metabolism of other medications. Nurses need to be aware of all medications patients may be taking, including over-the-counter and herbal preparations, because drug interactions with EIAEDs are common (see Figure 2). Patients require education regarding compliance with medication doses and schedules and strategies to avoid triggers that lower seizure threshold, such as stress, alcohol, or lack of sleep. Discussion with patients and families about safety issues such as driving restrictions and high-risk activities such as swimming alone should be included in the seizure education.

Venous Thromboembolic Events

The incidence of venous thromboembolism (e.g., deep vein thrombosis, pulmonary embolism) in patients with GBM is estimated to be as high as 60% during the first six weeks after craniotomy (Marras, Geerts, & Perry, 2000). Along with a diagnosis of GBM, possible risk factors of venous thromboembolism include length of surgery greater than four hours, immobility, age 60 or older, large tumor size, and chemotherapy (Marras et al., 2000). Symptoms of deep vein thrombosis include lower extremity edema, erythema, warmth, and a positive Homans' sign. Patients with any of these symptoms should be evaluated with an ultrasound to confirm if DVT is present. Pulmonary embolism symptoms can be quite subtle at first, with one of the early signs being slight tachycardia. Progressive symptoms include anxiety, dyspnea on exertion, tachypnea, chest pain, pain on inspiration, and oxygen desaturation. Pulmonary emboli are considered medical emergencies and patients and caregivers should be taught the symptoms to report. Low molecular-weight heparin, with fewer medication and food-related interactions than warfarin, often is the preferred method of anticoagulation for patients with neuro-oncologic conditions (Eisenson, 2007). It also may be used prophylactically in low doses to prevent venous thromboembolism.

Treatment Side Effects

Immediate postresection care of patients with GBM usually takes place in an intensive care setting. Neurologic assessments are done at regular intervals starting every 15 minutes for one hour, with the interval between checks increasing each hour.
consideration must be taken if any surgery is planned while on corticosteroids. Special attention is necessary during the immediate postoperative period. Nurses should individualize patient education and self-care measures during chemotherapy and radiation. Radiation can produce short-term side effects such as cerebral edema, localized skin irritation, and alopecia. Corticosteroids are used to control tumor-associated edema, and skin emollients or moisturizers soothe radiation dermatitis. Sunscreen and head coverings should be worn when patients are outdoors. Patients should be assessed for any symptoms or side effects, including neurologic changes, headache, and seizures activity, at weekly visits during radiation therapy.

Temozolomide commonly causes fatigue, myelosuppression, nausea, vomiting, anorexia, and constipation. Patients should take temozolomide on an empty stomach an hour before or two hours after eating. Premedication with a 5-hydroxytryptamine3 (5-HT3) receptor antagonist medication such as ondansetron or granisetron usually controls nausea and vomiting. Some patients (e.g., women, patients age 40 years or younger, who have low alcohol consumption, or with a history of motion sickness) might need additional antiemetics (Booth et al., 2007; Navari, 2003). Temozolomide capsules should never be opened, and caregivers should be instructed to use gloves when handling them. Constipation, a common side effect of both temozolomide and 5-HT3 medications, can be particularly problematic. A bowel regimen should be initiated that includes increased fiber and fluids, stool softeners, and laxatives to maintain regular function. Myelosuppression is a serious concern, particularly for women and older adult patients, while on temozolomide (Merrick & Co., Inc., 2010). Blood counts should be performed weekly and patients should be educated on neutropenic and thrombocytopenic precautions. Patients should be counseled to use contraceptives during chemotherapy because of potential teratogenic effects. If the treatment plan includes other chemotherapy agents such as carmustine or lomustine, nurses should individualize patient education and specific side-effect management accordingly.

Targeted therapies and antiangiogenic agents have the potential to cause side effects that differ from those commonly associated with chemotherapy. Bevacizumab may cause hypertension, VTEs, gastrointestinal perforation, proteinuria, and hemorrhage (Genentech, Inc., 2011). Delayed wound healing also may be a concern, particularly for patients on corticosteroids. Special consideration must be taken if any surgery is planned while on bevacizumab, and treatment may need to be held or schedules altered. Common side effects of targeted therapies can include diarrhea, rash, hand-foot syndrome, and fatigue.

Fatigue is a common symptom experienced by patients with GBM and varies among patients. Radiation therapy results in fatigue that is cumulative, with patients frequently reporting the most significant fatigue toward the end or following the course of treatment. To manage fatigue, exercise should be encouraged; even low-intensity exercise may positively affect QOL (Oldervoll, Kaasa, Knobel, & Loge, 2003; Porock, Kristjanson, Tinnelly, Duke, & Blight, 2000). Exercises can be tailored to fit each patient’s condition or disability and balanced with periods of rest. Rest and activity should be balanced so that priority activities of the patient and family can be performed (Barsevick, Newhall, & Brown, 2008). Patients with GBM may experience insomnia because of the stimulant effect of corticosteroids. If this occurs, the nurse should review the patient’s medication schedule. Taking the second dose of steroids with dinner or in the early evening, rather than at bedtime, may help reduce insomnia. Encouraging healthy sleep habits by maintaining regular sleep-wake patterns may be beneficial. If necessary, hypnotics may be helpful for short-term use. For some patients, medications such as methylphenidate or modafinil may be used to maintain wakefulness during the day.

Psychosocial Implications

The needs of patients with GBM and their families and caregivers are unique, multifaceted, and change throughout the course of illness. Treatment for newly diagnosed disease often is initiated rapidly, with a hospital admission for surgical resection on tumor discovery. Coping with the effects of a cancer diagnosis that carries a dismal prognosis while gathering and processing information to make complex treatment decisions can be overwhelming. In addition, physical, psychological, and cognitive sequelae from the tumor and subsequent treatment may impact coping. Patients with brain tumors frequently experience changes in their cognitive abilities, personality, and behavior, which may have a deleterious effect on QOL for patients and their families. Symptoms such as depression, aphasia, short-term memory loss, limited concentration, impaired judgment, loss of insight, and personality changes may be present. They may result directly from the tumor or resection and from supportive medications. Coping with symptoms can be extremely difficult for patients and families, particularly when dealing with confusion, delirium, hallucinations, or violent behavior. Patients may experience periods of exacerbation and improvement during the course of treatment. Nurses need to assess the unique situation of each patient and family and work with available resources, including medications, social work, and psychiatry, to determine appropriate interventions.

Halkett, Lobb, Oldham, and Nowak (2010) examined information and supportive care needs of patients diagnosed with...
high-grade gliomas. The main themes identified were the need for information, communication with health professionals, dependence on caregivers, and dealing with feelings of uncertainty (Halkett et al., 2010). Support for dealing with the uncertainty of the future also was identified as a major need by patients and their caregivers in a study by Janda et al. (2008), as well as help dealing with changes in mental or thinking abilities and behavior. Dealing with the loss of independence can be challenging. Patients with brain tumors may have inadequate insight and self-appraisal and may over-rate their ability to manage independently (Fox, Mitchell, & Booth-Jones, 2006). Many with cognitive and physical disabilities no longer are able to drive, work, live independently, or perform usual activities of daily living, including shopping, housekeeping, food preparation, medication management, and finance management. That may lead to role changes within the family unit, requiring caregivers to take on additional responsibilities. Patients typically struggle with the loss of control, trying to maintain normalcy and cope with their changing role within the family. Nurses can help explore ways to safely promote independence and suggest alternate ways to perform activities of daily living. Occupational, physical, and cognitive rehabilitation therapy, along with more specialized training, can be used to optimize function and may help facilitate return to a workplace, if applicable.

Oncology nurses must appreciate the new tasks and roles that family members and caregivers have assumed. Education about the disease process and side-effect management is important, but caregivers also need practical support and guidance to care for the patient’s physical disabilities and may need assistance in acquiring durable medical equipment, as well as home health and visiting nurse services. They also may need assistance with transportation and completion of financial and medication assistance, disability, and legal forms (e.g., advance directives, wills). Caregivers can become physically and emotionally overwhelmed, which can lead to poor health outcomes for themselves (Honea et al., 2008). Creating time during office visits for the nurse and caregivers to discuss difficulties, successes, and emotions can be helpful. Support groups specifically for caregivers also may be an appropriate option (see Figure 3). Arranging respite care and time away from caregiving to focus on the caregivers’ own emotional, physical, and spiritual needs should be encouraged.

Conclusion

GBM is a highly aggressive malignant tumor that affects all aspects of the patient’s and family’s lives. Advances in recent years lend hope for increasing QOL and survival. Oncology nurses are an instrumental part of the team and are patients’ closest allies during what may be the most difficult time in their lives. By effectively managing the symptoms of the disease and the side effects of treatment, oncology nurses foster patients’ hope and help them maintain their optimum level of function and QOL.

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