Brain tumors are classified as primary or metastatic depending on their site of origin. Primary brain tumors are those that arise from brain or meningeal tissue such as gliomas or meningiomas, respectively. Metastatic brain tumors are those that started in other organs such as the lung, breast or skin and spread to the brain, typically through the blood stream. The focus of this article will be the treatment of glioblastoma multiforme, commonly referred to as glioblastoma or GBM, the most common malignant primary brain tumor type.

According to the Central Brain Tumor Registry of the United States, the average annual incidence rate of primary brain and central nervous system tumors in the U.S. is approximately 21 per 100,000 and this translates into approximately 65,000 cases per year. The most common primary brain tumors are meningiomas, generally benign tumors that account for 35.8 percent of all cases. Meningiomas were discussed in the spring 2014 issue of NEUROtransmitter. The second most common primary tumors are gliomas, which account for 28 percent of tumors (Ostrom, 2013).

Gliomas and Glioblastomas
Gliomas are named and classified on the basis of their resemblance to normal glia, the support cells necessary for the proper functioning of neurons within the brain. For example, astrocytoma and oligodendroglioma tumors are comprised of cells that resemble normal astrocytes and oligodendrocytes, respectively. Using criteria devised by the World Health Organization, gliomas are also graded from I to IV for increasing degree of malignancy. Grades I and II are considered benign and grades III and IV are considered malignant. A grade IV astrocytoma, also known as glioblastoma multiforme, therefore consists of cells that resemble astrocytes and is highly malignant.

Glioblastomas account for 54 percent of gliomas and 16 percent of all primary brain tumors. Ninety-five percent of glioblastomas are thought to form spontaneously over a less than three-month period and this “primary GBM” subtype generally occurs in older patients (mean age 62 years) (Figure 1). Five percent of glioblastomas develop over the course of one to five years from the malignant progression of grade II and III gliomas and these “secondary GBM” tumors typically occur in younger patients (mean age 45 years) (Figure 1).

Primary and secondary GBMs have different sets of genetic mutations that lead to their formation and the male:female ratio of incidence for the two subtypes is 1.33 and 0.65, respectively (Ohgaki, 2007).

Surgical Removal of Glioblastoma
Once a suspected glioblastoma is identified on a magnetic resonance imaging (MRI) or computed tomography (CT) study of the brain,
surgically removing as much tumor as possible without worsening any existing or causing any new neurological deficits such as weakness or difficulty speaking should be the goal. In a study of 233 patients with newly diagnosed GBMs, patients who had 98 percent or more of their tumor removed survived a median of 13 months while those who had less than 98 percent of their tumor removed had a median survival of 10.1 months (Lacroix, 2001). Following surgery, patients are treated with concurrent temozolomide chemotherapy and radiation treatment followed by additional cycles of temozolomide alone. Surveillance MRI studies are obtained approximately every three months until recurrence of the tumor is identified.

Treatment of Recurrent GBM Tumors

While there is general consensus on the treatment of initially diagnosed GBM tumors as described above, there is no such agreement on the treatment of recurrent GBM tumors. The options include continued observation, additional cycles of cytotoxic chemotherapies, systemic biological therapies such as bevacizumab, or re-operation. In support of re-operation for selected groups of patients, a retrospective study of 143 patients from the National Institutes of Health (NIH) and Harvard Medical School reported that patients with good overall performance status and small to medium tumors in non-eloquent brain locations survived a median of 9.2 to 10.8 months following re-operation. In contrast, the median survivals of recurrent GBM patients following bevacizumab treatment alone was 7.2 to 9.2 months (Park, 2010). In a follow-up study of 97 patients from authors at the NIH and the Santa Barbara Neuroscience Institute (SBNI) at Cottage Health System, it was found that the median survivals of patients with gross total, near gross total, or incomplete resections of their recurrent tumors were 19.9 months, 10.6 months and 5.1 months, respectively (Yong, in press). Taken together, these two studies suggest that patients with recurrent GBM tumors who have favorable prognostic characteristics should undergo re-operation with the goal of removing as much tumor tissue as safely possible.

Re-operation for Recurrent GBM

The patient is a 65-year-old man who initially presented with headaches. A workup including a brain MRI revealed a gadolinium contrast-enhancing lesion on T1-weighted imaging in the right frontal lobe. He underwent a gross total resection which revealed the lesion to be a GBM. Surgery was followed by concurrent temodar chemotherapy and radiation therapy. Following the completion of radiation therapy, he underwent additional cycles of temozolomide. He was then followed with serial MRI scanning approximately every three months. Fifteen months after his initial surgery, he was found to have a recurrence of his tumor. Re-operation was performed with gross total resection of the tumor. He is still doing well two years later (Figure 2).

CASE STUDY

Figure 1. Contrast-enhanced axial MRI brain images. (A) and (B) This 61-year-old man was scanned at two different time points. In the first scan (A), there was no visible tumor. In the second scan (B) three months later, there was an obvious tumor in the left frontal lobe that turned out to be a GBM. (C) and (D) This 28-year-old woman was found to have a non-enhancing lesion, likely a low grade tumor, in the right frontal lobe (C), and no active treatment was undertaken. A repeat MRI scan performed 16 months later revealed an enhancing lesion that was confirmed to be a GBM following resection and pathologic analysis.

Figure 2. Contrast-enhanced axial MRI brain images. (A) Pre-operative image shows right frontal tumor. (B) Post-operative image shows resection cavity with no visible evidence of tumor.

To learn more about the Brain and Spinal Tumor Program or to request an appointment, contact Gary Milgram, Service Line Director, at (805) 569-7550 or gmlgram@sbcg.org

References: