All About Adult Gliomas

What is a glioma?

A glioma is a type of brain tumor that starts in the brain. It is a “primary brain tumor.” This is different than a brain tumor that has spread from another area of the body, which is called a metastasis. There are a number of different types of gliomas which are named based on the type of cells from which they arise: glioblastoma, astrocytoma, oligodendrogliomas, and ependymomas.

Gliomas are tumors that arise from “glial” cells. While neurons are the cells that carry signals, glial cells are the support cells in the brain that help keep neurons in place and working well. There are many more glial cells than neurons. There are many types of glial cells, including astrocytes, oligodendrocytes and ependymal cells. All types of glial cells arise from a common brain stem cell (stem cells are a type of cell that can turn into many different types of cells). Gliomas form when these immature stem cells mutate and grow out of control.

What causes gliomas and am I at risk?

According to American Brain Tumor Association, more than 79,000 new cases of brain tumors are diagnosed each year; but only about 23,880 of these are malignant (cancerous) tumors of the brain or spinal cord. Gliomas make up about 74% of malignant brain tumors. Men are at a slightly higher risk for developing a malignant brain tumor. The incidence of malignant brain tumors is small, with a lifetime risk of less than 1%.

There are few known risk factors for gliomas. Prior exposure to ionizing radiation, either to treat a medical condition (for example, a childhood cancer) or as a result of nuclear weapon exposure increases glioma risk. There are also several genetic conditions that predispose individuals to developing multiple types of cancer, including gliomas. Individuals with these genetic syndromes often have family members with a history of multiple cancers. Some of these genetic syndromes include Li-Fraumeni Syndrome, melanoma-astrocytoma syndrome, neurofibromatosis (types 1 and 2), Turcot's syndrome (types 1 and 2), and BRCA syndrome. If you have been diagnosed with multiple cancer types, or multiple cancer types run in your family, consider asking your healthcare provider about genetic testing.

Despite much press, cell phone use has not been shown to increase the risk of developing a brain tumor. Similarly, there is no conclusive evidence to suggest that aspartame (a sugar substitute), power lines, or industrial chemicals increase your risk of developing a brain tumor.

How can I prevent a glioma?

There are no known practices or lifestyle changes to prevent a glioma.

What screening tests are available?

There are no standardized screening recommendations at this time.

What are the signs of a glioma?

The signs and symptoms of a glioma are similar to those for all brain tumors. The most common symptoms include:

- Headache.
- Nausea and/or vomiting.
- Confusion.
- Seizures.
- Memory loss.
- Vision loss or blurred/double vision.
- Change in speech or language.
- Weakness on one side of the body.
- Difficulty with walking or balance.
- Personality changes.

These symptoms usually come on gradually over a period of days to months. Depending on what part of the brain the glioma is in, the symptoms may vary. Patients with brain tumors are also at higher risk of developing blood clots in the leg (deep vein thrombosis, DVT), lung (pulmonary embolism, PE), or brain (stroke). The symptoms of a brain tumor are quite general and can also be caused by a number of other, non-cancerous, conditions. If you have the symptoms above, you should be evaluated by your healthcare provider.

**How are gliomas diagnosed?**

When a patient has the signs and symptoms above, MRI (magnetic resonance imaging) with contrast of the brain is used to see whether a brain tumor is present and to characterize the tumor. MRI has largely replaced CT scans because MRI provides more detailed images of the brain and brain tumor and MRI does not use radiation. However, CT scans can be used in patients who cannot have an MRI (e.g. patients with metal objects in their body).

The type of brain tumor a person has is determined by a biopsy. A piece of the tumor is obtained, usually during a craniotomy, or via stereotactic (needle) biopsy, and then looked at under a microscope. This is done by a pathologist, a doctor who specializes in examining tissues under a microscope and making a diagnosis. A biopsy or surgical removal of the tumor, is needed to diagnose a brain tumor as a glioma.

**How are gliomas staged?**

Gliomas are classified as either low-grade or high-grade, based on their appearance under a microscope. The glioma's grade is based on the World Health Organization classification, and considers the cell type that makes up the tumor and how aggressive it looks under the microscope. The term "anaplastic" is used to describe aggressive tumors, which may grow more rapidly, invade surrounding brain, and tend to return after treatment. Gliomas are graded on a scale from I-IV, with grade I tumors growing the slowest and grade IV tumors carrying the worst prognosis. (I don’t know that I like that we say worst prognosis) Grade I gliomas, called pilocytic astrocytomas, are rarely seen in adults, and not talked about in this article. (More information about pediatric brain tumors).

Detailed Grading System from the World Health Organization is as follows:

**Grade I**
- Slow growing.
- Almost normal appearance under a microscope.

**Grade II**
- Relatively slow growing cells
- Slightly abnormal appearance.
- Can invade normal tissue.
- Can recur as a higher-grade tumor.

**Grade III**
- Actively reproducing abnormal cells.
- Abnormal appearance under a microscope.
- Invasions of adjacent normal tissue.
What are the treatments for gliomas?

Surgery is the primary treatment for gliomas since surgery is needed for staging. Often, a combination of therapies will be used for treatment, known as multi-modality treatment. See below for details regarding each type of treatment.

**Surgery**

There are 3 main goals of surgery:

- Stage the glioma.
- Improve symptoms by decreasing the size of the glioma.
- Remove all of the tumor if possible. If not, remove as much of the tumor as possible.

Surgery to diagnose and treat a brain tumor is known as acraniotomy. Most symptoms from gliomas are due to either increased pressure in the brain or compression of normal brain tissue. By removing some (if not all) of the tumor, pressure and compression are decreased, improving symptoms.

Whether or not the whole tumor can be removed is determined in part by where the tumor is in the brain. If a tumor is located in the speech and language or motor center, for example, complete removal of the tumor may not be possible without damaging speech, language, or movement. In other areas of the brain, it may be safe to remove the entire brain tumor. Consult with a neurosurgeon if you have questions about whether or not a tumor can be safely removed in its entirety.

**Chemotherapy**

Chemotherapy is the use of medications to kill cancer cells. Chemotherapy can either be a pill that you take by mouth or a liquid that is given through an IV into the bloodstream (intravenous). For chemotherapy to be able to kill glioma cells, it must be able to pass from the bloodstream into the brain. The brain is protected by the blood-brain-barrier, a specialized defense that prevents many toxins and chemicals (including some medicines) from entering and damaging the brain. Only certain chemotherapy medicines are able to cross the blood-brain-barrier.

The types of chemotherapy available to treat gliomas are based on the type of glioma being treated. With low grade astrocytoma and oligodendroglioma, medications used may include procarbazine, lomustine, vincristine (PCV) or temozolomide (TMZ). Anaplastic gliomas also are treated with PCV and TMZ; but recurrent anaplastic gliomas can also be treated with other chemotherapy medications including bevacizumab, irinotecan, carboplatin, cyclophosphamide and etoposide. Chemotherapy medications used to treat glioblastoma include TMZ, bevacizumab, irinotecan, carmustine, lomustine, carboplatin, PCV, cyclophosphamide and/or cisplatin. Ependymoma are often treated with carboplatin/cisplatin based regimens, etoposide, lomustine or carmustine, bevacizumab and/or temozolomide. Ask your healthcare provider about which chemotherapy (if any) may be right for you.

**Radiation Therapy**

Radiation therapy (radiotherapy) is commonly used to treat many different types of brain tumors. Radiation therapy is a “local” therapy, meaning the radiation is only aimed at the portion of the brain being treated. Gliomas are treated with fractionated radiation, which is the type of radiation therapy where a small dose of radiation is given to the area of the brain tumor 5 days a week, for several weeks. Over the treatment period, the amount of radiation to the tumor accumulates and causes the tumor cells to die.
The most common side effects of radiation to the brain are fatigue, hair loss, and memory loss. Other side effects depend on the location of the tumor. Fatigue and hair loss typically occur during the radiation treatment and last for about 4-6 weeks after radiation treatment is over. Memory loss develops over the years after radiation treatment, though you may notice some changes right away. It is often said that radiation to the brain is "like aging, but faster," meaning that the cognitive changes that normally happen with aging happen much sooner if you have had radiation. Ask your radiation oncologist about the details of your treatment what side effects you may be at risk for.

Other Treatments
Steroids, like prednisone or dexamethasone, may be a part of your glioma treatment. Steroids are anti-inflammatory medications that are used to decrease swelling in the brain that may develop from the tumor itself or its treatment. Some common side effects of steroids are infection, stomach ulcers or bleeding, weight gain, difficulty sleeping, and mood changes.

Another category of treatments used for gliomas (especially high-grade and recurrent glioma) is implants. These are used after surgical resection. Implants are typically small "seeds" or "wafers" which contain either chemotherapy or radiation. Implants are designed to bypass the blood-brain-barrier, by delivering treatment directly to the site of the tumor. Chemotherapy wafer implants (called Gliadel®) are small gel wafers containing the chemotherapy agent carmustine (BCNU). During surgery, a neurosurgeon places up to 8 wafers in the area where the tumor was (the so-called "tumor cavity"). Over the subsequent few days, the wafers release chemotherapy directly into the site of the tumor. The wafers dissolve completely in 2-3 weeks.

Brachytherapy is "internal" radiotherapy, meaning that the radiation source is inside the body, very close to the tumor. In the case of gliomas, brachytherapy can come in several forms, most commonly iodine-125 (125I) seeds and GliaSite®. GliaSite® is a radiation delivery system used for gliomas. During brain surgery, a neurosurgeon places a small balloon into the tumor cavity. A few weeks after the balloon is implanted, it is filled with liquid radiation, which delivers radiation to the surrounding tumor for a period of 3-6 days. After that time, the balloon and liquid are removed from the brain. Iodine-125 seeds are similar to GliaSite®; they too are placed by a neurosurgeon into the tumor cavity during brain surgery. The seeds also deliver radiation to the surrounding tumor, but, unlike GliaSite®, the iodine-125 seeds do not need to be removed.

Which treatment(s) is right for me?
Treatment depends on whether the glioma is low-grade or high-grade and the size and location of the tumor. There are different treatments used for recurrent high-grade gliomas, those gliomas which return despite treatment.

Low-grade glioma
If left untreated, low-grade gliomas will progress to become high-grade gliomas. There is no standard treatment for low-grade gliomas, though surgery to remove as much of the tumor as possible is recommended for most patients. If a young patient (less than 40 years old) has complete removal of their tumor, no additional treatment is generally needed. If a patient is older than 40 years or has incomplete surgical removal of their tumor, radiation is often recommended. Often, clinicians attempt to delay radiotherapy for as long as possible because patients with low-grade gliomas tend to be younger. Delaying (or avoiding) radiotherapy attempts to spare patients the memory loss and cognitive troubles that often develop after radiation to the brain. Chemotherapy is sometimes recommended for oligodendrogliomas, which tend to respond better to chemotherapy than astrocytomas.

High-grade glioma
The most common types of high-grade glioma are glioblastoma and anaplastic astrocytoma. High-grade gliomas cannot be cured. Quality of life issues are important to consider in the treatment of patients with high-grade glioma. Some quality of life issues to consider are fatigue, overall health, cognitive function, social function, emotional function, financial burden, future uncertainty, and insomnia. Symptom management and comfort concerns should be part of the conversation regarding the overall treatment plan. Measuring quality of life is important to fully understand the impact of a treatment on the disease; while the goal is improved survival, it must not be at the expense of quality of life.

A pivotal study (known as the Stupp trial) in treatment of glioblastoma found that combination treatment with temozolomide and radiation therapy significantly improved survival. These researchers found a group of patients who responded especially well to temozolomide – these patients all had a similar mutation in their tumors, causing the MGMT gene to be turned off. The MGMT gene is responsible for repairing DNA when it becomes damaged. When this gene is turned off, DNA damage
caused by temozolomide (through the process of alkylation) cannot be repaired, leading to cell death. The Stupp trial established the standard treatment for glioblastoma. While a standard treatment for anaplastic astrocytoma has not been so clearly established from research studies, most doctors treat anaplastic astrocytomas like glioblastomas.

Based on the Stupp trial, high-grade gliomas are first treated with surgery, removing as much tumor as is safe. After surgery, the standard treatment is a combination of fractionated radiotherapy for six weeks and temozolomide (Temodar). Temozolomide is given until the tumor begins to grow again (called tumor progression). In the setting of tumor progression, chemotherapy with bevacizumab (Avastin) is commonly used, though other chemotherapy drugs, including experimental treatments, may be tried.

**Recurrent High-Grade Glioma**

High-grade gliomas are often resistant to treatment or return after treatment. In fact, in excess of 90% of patients with glioblastoma will experience at least one recurrence. Patients whose tumors do not improve with radiation and temozolomide are candidates for participation in a clinical trial. Treatment options for recurrent high-grade glioma include surgery and chemotherapy. Some patients are offered re-resection along with chemotherapy wafers (Gliadel) or radioactive implants (e.g. GliaSite). Chemotherapy options include bevacizumab, irinotecan, carmustine, lomustine or platinum-based agents (e.g. cisplatin, carboplatin).

**Clinical Trials**

There are clinical research trials for most types of cancer, and every stage of the disease. Clinical trials are designed to determine the value of specific treatments. Trials are often designed to treat a certain stage of cancer, either as the first form of treatment offered, or as an option for treatment after other treatments have failed to work. They can be used to evaluate medications or treatments to prevent cancer, detect it earlier, or help manage side effects. Clinical trials are extremely important in furthering our knowledge of this disease. It is through clinical trials that we know what we do today, and many exciting new therapies are currently being tested. Talk to your provider about participating in clinical trials in your area. You can also explore currently open clinical trials using the OncoLink Clinical Trials Matching Service.

**Follow-Up Care and Survivorship**

Once a patient has been treated for a brain tumor, they need to be followed closely for a recurrence. At first, the patient will have follow-up visits fairly often. The longer they are free of disease, the less often they will have to go for checkups with examinations. The provider will decide when to obtain follow-up MRI scans.

Fear of recurrence, financial impact of cancer treatment, employment issues and coping strategies are common emotional and practical issues experienced by brain tumor survivors. Your healthcare team can identify resources for support and management of these practical and emotional challenges faced during and after cancer.

Cancer survivorship is a relatively new focus of oncology care. With some 15 million cancer survivors in the US alone, there is a need to help patients transition from active treatment to survivorship. What happens next, how do you get back to normal, what should you know and do to live healthy going forward? A survivorship care plan can be a first step in educating yourself about navigating life after cancer and helping you communicate knowledgeably with your healthcare providers. Create a survivorship care plan today on OncoLink.

**Resources for More Information**

**National Brain Tumor Society**

Aim to improve understanding of all brain tumors and transform research into new and effective treatments, as quickly as possible. Offers brain tumor information, related news and a blog. [http://braintumor.org/](http://braintumor.org/)

**American Brain Tumor Association**

Providing comprehensive resources that support the complex needs of brain tumor patients and caregivers, as well as the critical funding of research in the pursuit of breakthroughs in brain tumor diagnosis, treatment and care. [http://www.abta.org](http://www.abta.org)
Brain Science Foundation

Dedicated to finding a cure for meningioma and other primary brain tumors and to advancing the understanding of brain function as it relates to these tumors. Offers information on a variety of types of brain tumors as well as research initiatives. [http://www.brainsciencefoundation.org/Default.aspx](http://www.brainsciencefoundation.org/Default.aspx)

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