All About Pediatric Gliomas (Low and High Grade)

Brain tumors are the second most common tumor in children (20% of all pediatric cancers). Overall, the incidence of brain tumors is 4.84 cases per 100,000 children per year. Although some people say that the incidence of pediatric brain tumors has increased over the past few years, the incidence is most likely not rising – the increased numbers of brain tumors diagnosed has occurred because there is improved ability to detect these tumors.

Brain tumors can occur in any part of the central nervous system (CNS). The CNS includes the brain, the spinal cord and the fluid surrounding the brain and spinal cord, which is called the cerebrospinal fluid (CSF). The specific type of brain tumor is determined by what the tumor looks like under the microscope, which is called histology. The location of the tumor in the brain is also important. If the tumor starts in the brain, it is called a primary brain tumor. If the tumor starts elsewhere in the body and spreads to the brain, it is called a metastatic brain tumor. Metastatic means that the tumor has spread to other parts of the body, other than where it initially began. When a child is diagnosed with a brain tumor, the histology, location and stage of the tumor will help determine how the tumor will be treated.

Gliomas are the most common type of brain tumor in both children and adults. The word glioma encompasses many different tumor types, and gliomas come in different "grades." Gliomas are often categorized as "low-grade," meaning that the tumor cells look as if they are dividing more slowly under the microscope, or "high-grade," meaning that the cells look more aggressive under the microscope. Low-grade tumors can cause problems even when they are not malignant (cancerous) by pressing on the normal structures in the brain and causing symptoms. Gliomas develop from the abnormal growth of glial cells. A glial cell is a type of cell in the brain that surrounds the neurons, which are the cells that conduct electrical impulses to transmit information. Glial cells support and insulate the neurons. For example, an astrocyte is a special form of glial cell. Astrocytomas are a type of glioma that forms because of abnormal growth of astrocytes.

Approximately 60% of brain tumors in children occur in the infratentorial brain. The infratentorial brain is the lower part of the brain near the middle of the back of the head and includes the cerebellum and the brainstem. This is the part of the brain that controls movement and balance. The brainstem is the middle of the brain and connects the brain to the spinal cord. The brainstem controls breathing, movement of the eyes, passing on information about sensation and involuntary muscle movements. The supratentorial brain is the part of the brain that is above the cerebellum. The supratentorial brain includes the cerebrum, which is the largest part of the brain. This part of the brain controls thinking, emotions, problem solving, learning, talking, reading, writing and voluntary movement. Gliomas can be found in any part of the brain or spinal cord.

What are the types of pediatric gliomas?

Gliomas can either be low-grade or high-grade. Grading is done based on World Health Organization (WHO) criteria. The grade is a measure of how abnormal the tumors cells look under the microscope. High-grade tumors look very unusual. Low-grade tumors look different than normal brain cells, but they are not as abnormal-looking as high-grade tumor cells. The grade of the tumor also relates to how fast the tumor grows and affects prognosis. The WHO criteria were modified in 2016, and many gliomas are now classified both by their name, and by a description of their molecular or genetic characterization.

Pilocytic astrocytoma— This is a low-grade (WHO grade I) brain tumor that is made up of cells that are spindle-like in appearance. Pilocytic astrocytoma is the most common type of low-grade glioma. These types of gliomas often occur in the cerebellum and are called cerebellar pilocytic astrocytomas, though they can occur in any part of the CNS. The most common type of pilocytic astrocytoma is a juvenile pilocytic astrocytoma (JPA). JPA makes up 20% of pediatric brain tumors. Low-grade astrocytomas are usually slow-growing and are not found until they are very large and cause problems because of their size.

Anaplastic astrocytoma— This is a high-grade (WHO grade III) tumor. It is called anaplastic because the cells of the tumor do not have the structure of normal brain glioma cells. These tumors can grow in any part of the CNS. These tumors grow faster...
than low-grade gliomas and are more likely to recur even after treatment. They usually do not spread to other parts of the CNS.

**Glioblastoma multiforme** – This is a high-grade (WHO grade IV) tumor. These tumors can occur anywhere in the brain or spinal cord. While the tumors may start in one part of the brain, they sometimes spread to other areas in the CNS. These tumors are more aggressive, which means they grow faster than low-grade gliomas, and they also may grow back even after treatment.

**Diffuse midline glioma, H3 K27M-mutant (formerly called diffuse intrinsic pontine glioma [DIPG])** – This is a high-grade tumor that is found in the brainstem. These tumors account for 10% of all brain tumors in children. Patients with these tumors usually have neurologic changes that lead them to be diagnosed with their brain tumors.

**Optic pathway glioma** – This is a low-grade tumor that occurs in the optic nerve. The optic nerve is the nerve that goes to the eye.

**Tectal glioma** – This is a low-grade tumor that occurs near the brainstem.

**Oligodendroglioma** – This is a very rare type of low-grade glioma.

**Ganglioglioma** – This is a low-grade glioma. It has some features that look like glial cells and some features that look like neurons.

**Pleomorphic xanthoastrocytoma** – This is a low-grade glioma. The tumor often has a cyst as part of the tumor. Pleomorphic xanthoastrocytomas most often grow in the temporal lobe of the brain.

**Who gets gliomas, and how?**

Tumors are an abnormal growth of cells. In most cases we do not know why children develop brain tumors. There are some syndromes or genetic mutations that we know increases a child’s risk of developing a glioma. These syndromes include Li-Fraumeni syndrome, Turcot syndrome, and neurofibromatosis. Children with neurofibromatosis are specifically at higher risk for developing optic pathway gliomas. Another syndrome, tuberous sclerosis, can also lead to an increased risk of a type of low-grade glioma called subependymal giant cell astrocytoma. Sometimes children who have been treated for other types of cancer can develop brain tumors as a secondary cancer. In most cases, however, we do not know why a patient develops a brain tumor. Tumors begin when something goes wrong when cells divide to make new cells. This new abnormal type of cell grows quickly and creates a mass of abnormal cells. When a tumor develops in the brain, you cannot see it growing. Usually patients do not know that they have a brain tumor until the tumor is large enough to cause symptoms by pushing on normal structures in the brain.

**What are the signs and symptoms of gliomas?**

When brain tumors grow, they press on the normal parts of the brain and cause them to stop working properly. The signs and symptoms of a brain tumor depend on where the tumor is located in the brain. Gliomas can occur in any part of the CNS. Usually you cannot tell from the symptoms exactly what type of brain tumor is causing the problems. The most common symptoms are headaches and vomiting. Headaches that wake children up in the morning or headaches that are improved by vomiting are concerning for a brain tumor. Severe and frequent vomiting that does not seem to be part of a gastrointestinal bug are also concerning. Other symptoms of a brain tumor are changes in vision, such as double vision or blurry vision, hearing, or speech. If the tumor is in the optic pathway, it is more common to have vision loss or a bulging appearance to the eye (this is called proptosis). Children with brain tumors may become less steady while walking or have difficulty with balance. This is especially common in patients with astrocytomas because they often occur in the infratentorial brain. Children may become clumsy or have trouble holding objects or writing. Children may be confused or be more sleepy than normal. A child’s behavior may change if he or she has a brain tumor, including being irritable, and some young children do not meet their developmental milestones. In some cases the first sign of a brain tumor is a seizure. In infants, sometimes the head will get visibly larger if a baby develops a brain tumor. Children with high-grade gliomas tend to have symptoms for a shorter period of time because these tumors grow more quickly.

**How is a brain tumor diagnosed?**
History and Physical examination—The first step in diagnosing a brain tumor is evaluation by a healthcare provider. Healthcare providers ask many questions about changes in the child and about all of the signs and symptoms discussed above. They will ask if any other members of the family have had a brain tumor or any other cancer because there are some types of cancer that tend to run in families. The provider will perform a full physical examination, including a thorough neurologic examination. The neurologic examination evaluates the functioning of the brain and the spinal cord to look for any abnormalities. The neurologic examination will include checking a child’s mental status, coordination, senses and reflexes. If a child is old enough to walk, the examiner will check if the child is walking normally.

Imaging—Brain tumors are diagnosed by seeing the tumor on imaging of the brain. The two main kinds of imaging are Computed Tomography (CT) Scan and Magnetic Resonance Imaging (MRI). CT scans use x-rays to take a series of pictures of the brain from different angles. CT scans are very quick. Sometimes dye will be injected into the vein before the CT scan is performed to help improve the picture. A CT scan will often be the first type of imaging performed because it takes less time to do the test. If a CT scan shows a brain tumor, a patient will then have an MRI. MRI scans use magnets to take a detailed picture of the brain from multiple angles. A chemical called gadolinium is injected into the vein before the MRI. Gadolinium helps certain areas of the brain light up in the images to help with the diagnosis. An MRI scan can take multiple hours and the child needs to stay completely still during the scan. Sometimes children need medications to make them sleepy in order to not move during an MRI scan. A brain tumor will look like a mass or lesion in the brain that does not look like the normal brain tissue on the CT scan or MRI. Depending on the type of tumor, sometimes an MRI scan of the spine will need to be done to look for spread of the tumor, called metastasis, to other parts of the CNS.

Your physician may be able to determine a possible diagnosis based on the tumor’s appearance on a radiology scan. Gliomas often have a characteristic appearance on MRI. JPA usually looks well-circumscribed with clear margins, very little surrounding swelling, and cystic areas in the tumor. JPA also lights up brightly on certain types of MRI images (T2 images). Fibrillary astrocytomas do not have a clear margin on MRI. High-grade gliomas, such as anaplastic astrocytoma and glioblastoma multiforme, typically do not have clear edges and have a heterogenous appearance (parts of the tumor look different than other parts). There can also be swelling around the tumor and the normal brain may be shifted by the tumor pushing on the brain. Diffuse intrinsic pontine glioma (DIPG) is found in the brainstem and usually causes the brainstem to look enlarged.

Biopsy—The best way to make a final diagnosis about the type of brain tumor is looking at the tumor cells under a microscope to evaluate for cancer. In order to do this, surgery needs to be done to take a piece of the tumor out of the brain. This is called a biopsy. Specially trained doctors called pathologists will look at the tumor cells under a microscope to make a diagnosis of what the histology of the tumor is. Often the diagnosis is made when the whole tumor is removed during surgery instead of having a separate biopsy. Sometimes a brain tumor is located in a part of the brain where doing surgery would cause more problems than removing the brain tumor would solve. In those cases the diagnosis is made based on the MRI results and treatment is planned based on this imaging.

Lumbar Puncture—Children with high-grade gliomas may need a lumbar puncture (spinal tap) to look for spread of tumor to the spinal fluid (CSF). A lumbar puncture is when a needle is inserted into the lower back to get a sample of the spinal fluid. A pathologist will look at the cells from the CSF to look for any evidence of tumor.

How are gliomas in children staged?

Staging for brain tumors is dependent on the type of tumor. The staging will depend on if the tumor is just in the primary site or if it has spread to other parts of the CNS. Gliomas do not usually spread to other parts of the CNS; most often they only spread locally. The grade of the tumor is very important and this has been discussed above. Usually, gliomas are characterized as "localized," meaning that they have not spread, or "disseminated," meaning that they have spread elsewhere within the CNS.

How are pediatric gliomas treated?

Pediatric oncologists, who are doctors who treat cancer in children, work with each patient to develop an individualized plan to treat his or her tumor. Doctors use the histology and location to determine the specific treatment. Pediatric oncologists use information based on years of research trials performed to try to learn more about the best ways to treat cancer in children. Doctors work with families using this knowledge from how other patients have been treated combined with the goals and desires of each patient and his or her family to determine an individualized treatment plan for each patient.
The main options for treating brain tumors include surgery to remove the tumor, radiation and chemotherapy. If a child does not have symptoms from a tumor that is a low-grade glioma, sometimes the patient will be monitored closely and will not undergo treatment.

**Surgery**

If doctors think that a mass found in the brain on CT or MRI scan is a glioma, a surgeon will do a biopsy or surgery to remove the tumor. The primary treatment for both high and low-grade gliomas is surgery to remove (resect) as much of the tumor as can be taken out safely. Surgeons who remove brain tumors are called neurosurgeons. The neurosurgeon will use the CT or MRI scan to determine the surgical plan. The neurosurgeon may not know how much of the tumor can be safely removed until he or she sees what the brain tumor looks like during the surgery.

A gross total resection is when the whole tumor is removed during the surgery and no remaining tumor can be seen either during surgery or on MRI. A near-total resection is when more than 90% of the tumor is removed during surgery. A sub-total resection is when 51-90% of the tumor is removed during surgery. A partial resection is 10-50% of the tumor is removed during surgery.

The goal of surgery is to resect as much of the tumor as possible. However, studies have shown that it is not enough to just do surgery; most patients require chemotherapy and/or radiation to fully treat their brain tumors. Sometimes brain tumors are located in parts of the brain where doing surgery would cause more problems. This is the case in most optic gliomas and brainstem gliomas. In those cases children do not have surgery and are treated with radiation and/or chemotherapy.

**Radiation Therapy**

Radiation therapy uses x-rays or high-energy particles that are directed at a tumor to kill abnormal cells. The dose of radiation will depend on the type of tumor, the location of the tumor, and the age of the child. Radiation can have side effects, specifically causing long-term impairment in development in children who are very young. Radiation therapy is often delayed as long as possible in the youngest children to give them a chance to grow and develop as much as possible before receiving radiation. The doctors who provide radiation therapy are called radiation oncologists. Families will meet with their pediatric oncologists and radiation oncologists to determine the best plan for treatment with radiation.

There are two main types of radiation therapy that can be used: photon radiotherapy and proton radiotherapy. Photon radiotherapy is the traditional form of radiation therapy. Photon therapy refers to the use of x-rays that are aimed at the tumor, enter the body, travel through the tumor, and then exit from through the other side of the body. This means that the tissues on either side of the tumor are treated with radiation, in addition to the tumor itself. Proton therapy is different. Protons enter the body and are at their peak dose at the site of the tumor. This means that they do not give as much radiation to the tissues on either side of the tumor. This can be very helpful when radiation is given to an important part of the body, such as the brain. Only some cancer centers are able to use proton therapy currently, but it can be a good option for treating certain brain tumors in children.

**Chemotherapy**

Chemotherapy is medicine that is used to treat cancer. Chemotherapy can be given by mouth, into a vein, into the muscle or into the spinal fluid. After surgery, children with high-grade gliomas will often receive chemotherapy in addition to radiation therapy. Some children will receive chemotherapy before surgery to shrink the tumor and make it possible to remove more of the tumor. The chemotherapy agents that are currently used in treating high-grade gliomas are vincristine, carboplatin, temozolomide, lomustine, vorinostat, bevacizumab, and irinotecan. Some children with low-grade gliomas whose tumors cannot be removed surgically will receive chemotherapy as well.

**Treatment of specific types of gliomas**

**Low-grade gliomas (pilocytic astrocytoma and fibrillary astrocytoma)**—For patients with low-grade gliomas, surgery may be the only treatment that is needed. If a child has a gross total resection, he or she does not need any other treatment. If there is not a gross total resection or if the tumor grows after surgery, a child may need radiation or chemotherapy. This decision will be made based on how much of the tumor remains, the post-operative symptoms of the child, and the age of the child.

**High-grade gliomas (anaplastic astrocytoma and glioblastoma multiforme)**—Most patients with high-grade gliomas have at least part of their tumor removed surgically. For some patients, however, the tumor cannot be fully removed safely. Children with high-grade gliomas need additional treatment after surgery due to the aggressive nature of the tumor. This additional
therapy is to treat remaining microscopic tumor cells that are presumed to be present even after surgery. Most children will undergo high-dose radiation therapy to the tumor site after surgery. This radiation is usually given over a 6 week period and is combined with weekly chemotherapy. Children often receive further maintenance chemotherapy after radiation is completed.

**Optic pathway glioma**—While these are low-grade tumors, the location of these tumors in the optic pathway can make it difficult to surgically remove the tumor without causing significant long-term side effects. These patients receive a combination of chemotherapy agents to treat their tumors.

**What happens if the glioma comes back?**

Unfortunately, gliomas can recur after treatment. If the tumor recurs, the plan for treatment will be very customized, and will depend on where the new tumor is and how the child was treated initially. Some children who have recurrent glioma will receive high-dose chemotherapy followed by autologous stem cell transplant. Other children may receive treatment as part of a phase I clinical trial evaluating new chemotherapy options.

**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 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**

After treatment for childhood cancer, the patient will be followed closely to monitor for the cancer coming back, to help them heal from ongoing side effects, and to help them to transition to survivorship. Initially they will be seen often and have ongoing tests to monitor their health. As time goes on, these visits and testing will become less frequent. The oncology team will discuss each patient’s individual follow up plan with them.

Survivors often wonder what steps they can take to live healthier after cancer. There is no supplement or specific food you can eat to assure good health, but there are things you can do to live healthier, prevent other diseases, detect any subsequent cancers early and work with the social and emotional issues, including insurance, employment, relationships, sexual functioning, and fertility, that a prior cancer diagnosis sometimes brings with it. Your oncology team is there to support you and can help you find support resources.

It is important to have a plan for who will provide your cancer-focused follow up care (an oncologist, survivorship doctor or primary care doctor). Talk with your oncology team about developing a survivorship care plan. If you would like to find a survivorship doctor to review your history and provide recommendations, you can contact cancer centers in your area to see if they have a survivor's clinic or search for a clinic on OncoLink's survivorship clinic list.

**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.


**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.
Pediatric Brain Tumor Consortium: research organization devoted to the study of tumor biology and new therapies for primary CNS tumors of childhood.

Pediatric Brain Tumor Foundation

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