

A Patient Guide to Brain Tumors

Every year, approximately 17,000 patients are diagnosed with cancer of the brain. For children and adolescents these tumors are among the most common cancer-related causes of death. However, most commonly affected are adults in their 5th decade of life. In this population as many as 2 in 10,000 individuals are afflicted each year - a figure which has risen over the last decades. Brain tumors are now the second fastest growing cause of cancer death among those over the age of 65. Unlike lung cancer and melanoma, which are the first and third on that list, there are no known lifestyle or behavioral changes that will reduce the risk of developing a brain tumor.

High-grade gliomas account for over three-quarters of these tumors. As these tumors are rare and therapies complicated to perform, patient care has shifted to tertiary care facilities such as the Yale Brain Tumor Center able to provide multidisciplinary care including surgery, radiation and chemotherapy.

In addition to patients with primary cancer of the brain there are 80,000 more diagnosed with metastatic (or secondary) tumors that have spread to the brain from elsewhere in the body. The Yale Brain Tumor Center provides not only the latest therapeutic approaches to brain metastases but also gives patient access to a large number of subspecialists at the Yale Comprehensive Cancer Center covering the whole spectrum of systemic cancer. Office visits are coordinated in a way that minimizes the number of visits to New Haven and the length of the overall stay.

Primary brain tumors are still classified based on their resemblance to normal cells and structures of the nervous system. The nervous system consists of nerve cells – the cells that form the neural network that enables us to move, feel, see, hear, smell, taste and think – and supporting cells – the so called ‘glial’ cells which are comprised of astrocytes, oligodendrocytes, ependymal cells and cells of the choroid plexus. Astrocytic tumors (‘astrocytoma’) predominate, followed by ‘oligodendroglioma’, and mixed tumors. Least common are growths in proximity to the ventricles and choroid plexus (‘choroid plexus papilloma’ and ‘ependymoma’).

Brain tumors are also classified into four grades according to their anticipated aggressiveness. Grade I and II are considered ‘low grade’, grade III and IV ‘high grade’. ‘Low-grade glioma’ is a descriptive term and does not always imply a benign clinical course. A ‘benign’ infiltrating astrocytoma of the brainstem can lead to disability and death; a similar lesion in the visual pathway causes blindness and ‘low-grade glioma’ within the spinal cord can produce irreversible paralysis. ‘High grade’ tumors have a tendency to grow more rapidly and require multi-modality therapy (surgery, radiation and/or chemotherapy). ‘Low grade’ tumors can evolve into a high grade tumor and thus follow-up with your doctor in regular intervals is warranted.

Specific Brain Tumors

A. Astrocytic Tumours

Low grade Astrocytomas

Astrocytomas are derived from brain or spinal cord astrocytes. The best therapeutic approach is still controversial. We provide biopsy or tumor removal, if possible, to establish a diagnosis as early as possible. Radiation or chemotherapy is reserved for patients with astrocytomas that can not be removed due to their location in critical areas of the brain, cause symptoms such as seizures or weakness or those that show early signs of transformation into a 'high grade' tumor.

Pilocytic Astrocytoma

Most pilocytic astrocytomas are located in the cerebellum, the coordination center of the brain. For these, complete surgical removal is often feasible and potentially curative. The remainder grows in areas of the brain called the hypothalamus, the optic chiasm or the brainstem. These structures are crucial for normal vision and endocrine function (water and electrolyte household, sexual functions, or temperature control). Tumors growing within these areas can not be completely removed. However, pilocytic astrocytomas usually grow very slowly if at all and thus radiation therapy is only provided if severe symptoms are present.

Pleomorphic Xanthoastrocytoma

Pleomorphic xanthoastrocytoma (PXA) is a rare, usually benign superficial glioma. Complete resection is feasible in most patients and potentially curative.

High grade Astrocytomas

Anaplastic Astrocytoma, Glioblastoma multiforme

High-grade gliomas are the most common primary brain tumors in adults. Following diagnosis, treatment should not be delayed due to their rapid growth. Treatment usually consists of surgical removal of the tumor, radiation and chemotherapy.

Radiation therapy is the single most effective treatment for malignant glioma. Standard treatment consists of so called 'fractionated external beam irradiation' provided five days a week for six weeks.

Chemotherapy represents an additional treatment option for high-grade astrocytic tumors. Since the early 1970s a group of drugs called 'nitrosoureas' (BCNU or carmustine, CCNU or lomustine) have been the standard chemotherapeutic agents. Temozolomide is an alternative to these classical agents. It is typically given for five days every four weeks but various modifications to this protocol exist. High-grade astrocytomas can grow resistant to this type of chemotherapy. Alternative drugs include, among others, cisplatin,

carboplatin, etoposide, and irinotecan. In addition, new treatments are being tested in clinical trials.

Gliomatosis cerebri

Diffuse infiltration of large areas of the brain with glioma cells is denoted as gliomatosis cerebri. As the tumor can not be resected, only a biopsy is obtained. Radiation therapy is given if the tumor causes symptoms. Chemotherapy is provided if symptoms deteriorate after radiation.

B. Oligodendroglial Tumours

Oligodendroglioma. Oligoastrocytoma.

Surgical tumor removal is the treatment of choice for ‘low grade’ and ‘high grade’ oligodendrogliomas whenever feasible. These tumors also respond to irradiation and chemotherapy, such as a combination of drugs called ‘PCV’ which stands for procarbazine, lomustine and vincristine. We provide PCV therapy to benign oligodendrogliomas that cannot be resected, are symptomatic, or show features of a more aggressive tumor. It is not clear whether this therapy should be given before radiation is provided; but this has been our approach in many patients.

Oligoastrocytomas are mixed glial tumors that contain cells resembling astrocytes and oligodendrocytes. Treatment is identical to the ‘pure’ oligodendrogliomas.

Anaplastic Oligodendroglioma. Anaplastic Oligoastrocytomas.

Patients whose oligodendroglial tumor shows ‘high grade’ features are usually treated with surgery, chemo- and radiation therapy.

C. Ependymal Tumours

Ependymoma, Anaplastic Ependymoma

Ependymomas can occur anywhere within the central nervous system. In adults, ependymomas are usually located within the spinal cord but they can also be found in the brainstem and the balance center (the cerebellum) or even within the hemispheres of the brain.

Complete surgical removal should be attempted whenever feasible and may cure the patient with a low-grade ependymoma. Patients with residual tumors that cause symptoms, those with relapsing tumor, or those with ‘high-grade’ tumors benefit from radiation therapy. Chemotherapy is reserved for patients whose ‘high-grade’ tumors are resistant to other types of treatment.

D. Choroid Plexus Papilloma

Choroid plexus papillomas are tumors of childhood. In adults, they are extremely rare. Choroid plexus papilloma is derived from the structure that produces cerebrospinal fluid, the fluid that surrounds the brain and fills the ventricles, large spaces within the brain. Surgical resection is the treatment of choice and potentially cures the patient.

E. Neuronal and mixed Neuronal-glial Tumours

Ganglioglioma and Gangliocytoma

Gangliogliomas contain two cell populations: nerve cells ('gangliocytes') and glial cells. Prognosis after total removal is excellent. A small portion of tumors that can not be removed completely can transform into a 'high-grade' tumor which requires radiation therapy and chemotherapy.

Central Neurocytoma

Central neurocytoma is a nerve cell tumor occurring in young adults located in the ventricles of the brain. The mainstay of treatment is surgical removal. The tumor adheres to adjacent structures and thus some tissue is usually left behind. Prognosis is excellent even in patients in whom total removal could not be achieved. Few tumors are more aggressive and require radiation therapy.

F. Tumors of the pineal gland

The pineal gland is a structure at the base of the brain that is involved in maintaining our circadian rhythm. Tumors of this gland are rare in adults and a large number of them are of 'low grade'. Complete tumor resection is attempted. Patients with 'high grade' tumors require radiation therapy. The use of chemotherapy is restricted to patients with high-grade tumors that disseminate along spinal fluid pathways or recurrent tumors.

G. Peripheral Neuroblastic Tumours

Aesthesioneuroblastoma

Aesthesioneuroblastoma is a malignant tumor arising from the neuroepithelium of the upper nasal cavity – the receptors for smell. It frequently invades the skull and sometimes even the brain or its coverings through the cribriform plate, a thin bony plate that separates the nasal cavity from the brain. Frequently surgical removal is followed by radiation therapy. Radiation may not be necessary in low-grade tumors that can be taken out completely. Patients with tumors that can not be controlled with surgery and radiation, recurrent or disseminated tumors, or high-grade tumors should be treated with

chemotherapy. Usually a combination of drugs is given almost always containing a drug called cisplatin. Some centers offer patients radiation or chemotherapy before surgery in order to facilitate complete removal of the tumor in the operating room. Some patients may be eligible for radiosurgery.

H. Embryonal Tumors

Medulloblastoma

Medulloblastomas are rare tumors in adults. The majority of patients present before 40 years of age. The tumor is restricted to the posterior fossa – the back and lower portion of the skull in more than half of adult patients. Dissemination into the spinal fluid is seen in one third of cases. As opposed to most other primary brain tumors, medulloblastoma can spread to places outside of the nervous system, especially bone.

The neurosurgeon tries to remove the tumor completely but this can frequently not be accomplished as the tumor infiltrates adjacent vital structures. After surgery, craniospinal irradiation is given (radiation to brain and spine). Chemotherapy benefits high risk patients, i.e. those with residual tumor after resection or spread into the spinal fluid. Combination of several chemotherapy drugs such as cisplatin, cyclophosphamide, nitrosoureas or etoposide have been most successful. Chemotherapy is usually given before radiation since the blood stem cell reserve after craniospinal irradiation may be exhausted. Chemotherapy may have a role in patients with low-grade medulloblastomas as well.

Supratentorial Primitive Neuroektodermal Tumors

Supratentorial primitive neuroektodermal tumours are much less common than medulloblastomas. The therapeutic approach to these tumors is similar to medulloblastoma. Surgical removal provides the diagnosis and reduces the tumor burden. This is followed by a combination of radiation and chemotherapy.

I. Tumors of cranial and peripheral Nerves

Schwannoma, Neurofibroma

Schwannomas and neurofibromas are benign tumors of the peripheral nerve sheath – the insulation of nerves. Schwannomas arising from cranial nerves are much less common. Schwannomas most commonly affect the vestibular division of the eighth cranial nerve (acoustic Schwannoma) – the nerve that transmits information from the receptors for movement to the brain. The majority of acoustic Schwannomas remain undetected. Incidentally found tumors with typical MRI appearance and location as well as clinically stable tumors with minimal symptoms can be followed with serial MRI scans. Symptomatic tumors are amenable to microsurgical resection or stereotactic radiosurgery.

Malignant Peripheral Nerve Sheath Tumour

Malignant peripheral nerve sheath tumor (MPNST) is a rare neoplasm of peripheral nerves including cranial nerves. Wide surgical excision of the tumor and the tissue surrounding it is the primary treatment of choice. Radiation therapy before or after surgery is clearly of benefit. 'Brachytherapy' – the temporary placement of a source of radiation close to the tumor - intraoperative irradiation in addition to external beam radiation may improve outcome in selected patients and avoid amputation of a limb. 20 to 40 % of patients are given chemotherapy as part of their initial treatment. Chemotherapy does not seem to have a role in the initial treatment of MPNST for patients without metastases in whom gross total tumor resection is accomplished.

J. Meningeal Tumours

Meningioma

Meningiomas are usually benign tumors of the covering of the brain or spinal cord – the meninges. Treatment is dependent upon location, appearance on imaging studies, the patient's symptoms and age. Incidentally found asymptomatic small meningiomas can be safely watched with serial MRI scans. In symptomatic meningiomas overlying the hemispheres of the brain, surgical resection is the primary treatment and can be curative. Challenging are tumors invading blood vessels and tumors arising from the base of the skull. Less aggressive conventional surgery in association with radiosurgery reduces treatment-related complications.

Atypical (6 % of all meningiomas) and malignant meningiomas (2 %) require a combination of surgery, radiation and sometimes chemotherapy.

Haemangiopericytoma

Intracranial hemangiopericytoma is a rare neoplasm of the covering of the brain and spinal cord. In spite of treatment, these tumors frequently grow back in the same place where they started or spread to other body parts (most commonly bone and liver). Late recurrences beyond five years of initial treatment are frequent. Surgical removal is the primary treatment of choice. Radiation therapy appears to reduce the local recurrence rate. Chemotherapy may benefit the patient with metastases or local therapy-refractory disease.

K. Tumours of the hematopoietic System

Primary Central Nervous System Lymphoma (PCNSL)

PCNSL is a very aggressive tumor of B-lymphocytes (the antibody-producing cells of the immune system). Chemotherapy with a drug called methotrexate alone or in combination

with other agents such as cytosine arabinoside or thio-TEPA is currently the single most effective treatment for PCNSL.

In patients whose lymphoma has spread to the spinal fluid, chemotherapy may also be given into the spinal fluid. This is usually done through a reservoir that is placed underneath the skin of the scalp ('Ommaya reservoir'; see the chemotherapy section of this website).

An increasing number of brain tumor physicians save radiation therapy for recurrent tumors or those that don't respond to chemotherapy alone. Radiation is very effective but used without chemotherapy, tumor relapse occurs within less than a year.

Lymphoma diffusely infiltrates the brain. Thus it can not be removed surgically. However, tissue needs to be obtained to make the diagnosis. This is accomplished through stereotactic biopsy (see the surgical section of this website).

Even after combined treatment with radiation and chemotherapy, the relapse rate of PCNSL is high. Regular follow-up visits and brain scans are necessary in order to diagnose relapsing disease early. Over the last ten years, the prognosis of patients with this disease has dramatically improved.

Patients with the Acquired Immune Deficiency Syndrome (AIDS) are predisposed to developing PCNSL in the advanced stage of their disease. A severely compromised immune system and concomitant opportunistic infections frequently precludes them from receiving chemotherapy. Thus whole brain radiation therapy has been the standard treatment for PCNSL in AIDS patients. The introduction of highly aggressive antiretroviral therapy (HAART) has led to a marked reduction in the number of AIDS patients who suffer from PCNSL and an increase in the number of patients eligible for chemotherapy.

L. Germ cell Tumours

Germ cell tumors of the central nervous system are extremely rare in adults (less than 0.1 % of primary brain tumors). 90 % of patients are diagnosed before age 20. They are much more common in East Asia. The most common germ cell tumor occurring within the CNS is called 'germinoma'. This tumor is identical to certain tumors of the testis and the ovary. Much less common are 'non-germinomatous' germ cell tumors which are called teratoma, embryonal carcinoma, yolk sac tumor (endodermal sinus tumor), choriocarcinoma, and mixed germ cell tumors. Germ cell tumors preferentially affect 'midline' structures of the brain such as the region of the pituitary gland – an important hormone secreting structure at the base of the brain - and the pineal gland, an organ involved in the regulation of our daily rhythm.

Treatment for germ cell tumors depends on the tumor subtype. Commonly surgical resection or biopsy is followed by radiation therapy. Chemotherapy given before irradiation can shrink the tumor and reduce the size of the radiation field.

M. Tumours of the sellar Region

Craniopharyngioma

Craniopharyngioma is a benign tumour derived from a developmental remnant called Rathke's pouch. Microsurgical resection is the primary treatment in symptomatic cases. Radiation may benefit patients whose tumor can not be completely removed.

Pituitary Adenoma

The pituitary gland is a structure at the base of the brain where important hormones regulating growth, thyroid function, sexual function and electrolyte/water balance are secreted into the blood stream. Adenomas are benign tumors derived from this gland. Surgical removal is the treatment of choice for pituitary adenomas above a size of 1 cm (a third of an inch) in diameter, and those causing damage to adjacent structures of the brain (such as the visual pathway). Radiation therapy is given to patients who can not be operated upon and or in whom only partial removal was achieved. The majority of patients treated with surgery and radiation require replacement of pituitary gland dependent hormones. Treatment with medication – so called 'dopamine agonists' (bromocriptine, cabergoline, quinagolide, pergolide) - can lead to a reduction in tumor size and improvement of symptoms.