Primary malignant brain tumors in adults exist in a dizzying array of forms. Find out about the types of tumors, their signs and symptoms, treatment options, and effective patient management.

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The author has disclosed that she has no significant relationships with or financial interest in any commercial companies that pertain to this educational activity.

ONE OF THE most chilling pronouncements anyone can hear is, “You have a brain tumor.” The fear this declaration causes the patient is often justified, especially when the tumor’s malignant, invasive, fast-growing, and life-threatening. Existing treatments can be ineffective.

Tumors that originate in the brain vary widely by tissue type, site of occurrence, growth potential, tendency to progress, tendency to recur, and treatment response. According to the Pediatric Brain Tumor Foundation of the United States, brain tumors are the deadliest of childhood cancers. And just because a brain tumor is benign doesn’t mean it’s harmless; a benign tumor in the wrong place can be deadly. Regardless of their characteristics and point of origin, however, malignant brain tumors have the highest morbidity and mortality rates.

Tumors originating from structures within the brain are called primary brain tumors. Those that spread from other areas in the body to the brain are called secondary, or metastatic, brain tumors. In this

By the numbers
Primary brain tumors represent 1.4% of all cancers diagnosed in the United States. About 18,500 primary malignant brain tumors are diagnosed each year. If you include all primary brain tumors, the number rises to around 41,000 new cases each year. Almost 13,000 deaths annually are caused by brain tumors.
Let’s take a closer look at what’s inside you.

Central processing unit
The brain consists of soft, spongy tissue divided into three major structures: the cerebrum, the cerebellum, and the brain stem. It’s covered and protected by the skin, the skull, and the meninges. Cerebrospinal fluid bathes the tissue and cushions it from shocks.

The outer layer of the cerebrum, the cerebral cortex, consists of unmyelinated nerve fibers called gray matter. Within the cerebrum are myelinated nerve cells called white matter. Basal ganglia, which control motor coordination and steadiness, are found in the white matter.

The undulating surface of the cerebrum is made up of gyri (convolutions) and sulci (creases). The cerebrum has a right and left hemisphere. The corpus callosum, a mass of nerve fibers, bridges the hemispheres, allowing communication between corresponding centers on each side. Some of the large sulci divide the surface into lobes: the frontal, the left and right parietal, the left and right temporal, and the occipital. The lobes are named after the cranial bones that cover them.

The cerebellum is underneath the back part of the cerebrum. It also has two hemispheres, each having an outer cortex of gray matter and an inner core of white matter. This part of the brain maintains muscle tone, coordinates muscle movement, and controls balance.

The brain stem lies just below the cerebrum, in front of the cerebellum. It runs from the cerebrum and connects to the spinal cord, and it consists of the midbrain, the pons, and the medulla oblongata. Its function is threefold: (1) to mediate autonomic cardiac, respiratory, and vasomotor function; (2) to provide two-way communication lines for nerve signals; and (3) to serve as the origin for 10 of the 12 pairs of cranial nerves.

Where the trouble starts
Primary brain tumors are classified according to histology (tissue of origin), as follows:

- Tumors originating in neuroepithelial tissue
  - astrocytomas
  - glioblastomas
  - oligodendrogliomas
  - mixed gliomas
  - ependymal tumors
- Tumors originating in cranial and spinal nerves
  - central nervous system lymphoma
- Tumors of sellar region
  - pituitary adenomas
  - pituitary carcinomas
  - craniopharyngiomas
  - chordomas, chondrosarcomas.

Anatomy of the brain
Making the grade

Because the tumor-node-metastases (TNM) staging system used for many other cancers doesn’t work very well for brain tumors, classification is based on alternate systems. Following are two of the most widely used: the World Health Organization (WHO) classification of nervous system tumors and the National Cancer Institute’s (NCI) grading system for adult brain tumors.

<table>
<thead>
<tr>
<th>WHO grade</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Discrete lesions with low proliferative potential. May be curable with surgical resection.</td>
</tr>
<tr>
<td>II</td>
<td>Infiltrating lesions that are low in mitotic activity but recur. Some tumor types tend to progress to or recur at higher grades of malignancy.</td>
</tr>
<tr>
<td>III</td>
<td>Lesions with histologic evidence of malignancy in the form of mitotic activity, clearly expressed infiltrative capabilities, and anaplasia.</td>
</tr>
<tr>
<td>IV</td>
<td>Lesions that are mitotically active, necrosis-prone, and associated with a rapid preoperative and postoperative evolution of disease.</td>
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</table>

<table>
<thead>
<tr>
<th>NCI grade</th>
<th>Characteristics</th>
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<tbody>
<tr>
<td>I</td>
<td>The tumor grows slowly, has cells that look similar to normal cells, and rarely spreads into nearby tissues. It may be possible to remove the entire tumor by surgery.</td>
</tr>
<tr>
<td>II</td>
<td>The tumor grows slowly, but may spread into nearby tissue and may become a higher-grade tumor.</td>
</tr>
<tr>
<td>III</td>
<td>The tumor grows quickly, is likely to spread into nearby tissue, and the tumor cells look very different from normal cells.</td>
</tr>
<tr>
<td>IV</td>
<td>The tumor grows very aggressively, has cells that look very different from normal cells, and is difficult to treat successfully.</td>
</tr>
</tbody>
</table>

The diencephalon is the part of the brain located between the cerebrum and the mid-brain. It consists of the thalamus, the hypothalamus, the subthalamus, and the epithalamus, which lie deep in the cerebral hemispheres. All sensory information (except for olfactory information) has to check in at the thalamus before it can be transmitted appropriately to the brain. The hypothalamus helps to power autonomic functions, like regulating body temperature, hunger, hormone output, and the sleep/wake cycle.

Those are the parts. Now let’s briefly look more closely at the types of cells that make up the various brain structures.

The nervous system contains two types of cells: neurons and glial cells. The neurons are the basic anatomic and functional units of the nerves. The glial cells provide nourishment, structural support, and protection for the neurons. Within the brain and spinal cord, glial cells surround nerve cells and hold them in place. They’re subdivided into four main types: astrocytes, oligodendrocytes, ependymal cells, and microglia. Astrocytes and oligodendrocytes are specific types of neuroglial cells (nonneural supporting elements). Oligodendrocytes form myelin in the central nervous system (CNS).

Now that we’ve got the architecture in place, it’s time for a look at what can go wrong when a tumor arises in one or more of these structures.

Invasion force

Experts haven’t yet found any positive causes or risk factors for primary brain tumors. In a few rare hereditary syndromes—NF1, NF2, Turcots, Gorlins, tuberous sclerosis, and Li-Fraumeni—
there’s a genetic link to brain tumor development. Links to environmental exposures are under scrutiny; only one, exposure to ionizing radiation, is known to increase the risk of a primary brain tumor.

Primary brain tumors are classified according to the tissue of origin or histology—how it looks under a microscope (see Where the trouble starts). Two grading systems are commonly used (see Making the grade). The higher the grade, the more aggressive the tumor will be. Tumors often contain several grades of cells: the highest grade determines the grade by which the tumor is classified. Further classification is based on genetic tumor markers and molecular biologic abnormalities.

The signs and symptoms of a brain tumor depend on its size, type, and location. Tumors can arise from the brain tissue itself or from the meninges, pituitary gland, or cranial blood vessels (see A glossary of common tumor types). Symptoms, often characterized by insidious onset, are typically caused by an increase in intracranial pressure (ICP) and blockage of cerebrospinal fluid. Some of the most common signs and symptoms include:

- frequent headaches
- decreased motor strength and coordination
- seizures
- altered vital signs
- vomiting with or without nausea
- papilledema
- anorexia
- changes in mood/personality
- changes in the ability to think and learn.

Most patients present with a headache that won’t go away with pain medication. Headaches occurring on awakening can be an early symptom of brain tumor. They may be associated with projectile vomiting, which suggests an increase in ICP. The headaches may be dull or sharp and, as the ICP rises, tend to be frontal or occipital.

Some patients have changes in mental status, mood, or personality. They may also suffer memory loss, lose the ability to concentrate, or exhibit focal neurologic signs.

### A glossary of common tumor types

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gliomas (account for 40% to 50% of</td>
<td>Tumors of the neuroepithelial/glial cells</td>
</tr>
<tr>
<td>intracranial neoplasms)</td>
<td></td>
</tr>
<tr>
<td>• Astrocytomas</td>
<td>Overgrowth of astrocyte cells (the brain’s connective tissue)</td>
</tr>
<tr>
<td>• Oligodendrogliomas</td>
<td>Overgrowth of oligodendrocyte cells with calcification</td>
</tr>
<tr>
<td>• Ependymomas</td>
<td>Overgrowth of the ependymal cells</td>
</tr>
<tr>
<td>• Mixed gliomas</td>
<td>Two or more cell types within a tumor</td>
</tr>
<tr>
<td>• Medulloblastomas</td>
<td>Most common pediatric malignant tumor. Rapid growth pattern, highly invasive with a high risk of metastases</td>
</tr>
<tr>
<td>Meningiomas</td>
<td>Arise from the linings (meninges) of the brain and can involve the skull</td>
</tr>
<tr>
<td>Peripheral nerve tumors</td>
<td>Include acoustic neuroma, schwannoma, and Von Recklinghausen’s (type 1) neurofibromatosis and type 2 neurofibromatosis</td>
</tr>
<tr>
<td>Pituitary adenomas</td>
<td>Can be secreting or nonsecreting</td>
</tr>
<tr>
<td>Germ cell tumors</td>
<td>Dermoid cysts, epidermoid cysts, pineal tumors, and chordomas</td>
</tr>
<tr>
<td>Hematopoietic tumors</td>
<td>Primary malignant lymphomas</td>
</tr>
</tbody>
</table>

I haven’t been myself lately!
Delirium and dementia are often indicators of a brain tumor. These symptoms are poorly understood, and they can cause distress for the patient and his family.

Brain tumors can produce irritation that causes seizures. Common types of seizures that arise from brain tumors include simple focal, complex partial, and generalized tonic-clonic. Simple focal seizures are localized; that is, they’re produced in a specific part of the brain. These seizures involve simple sensory or motor functions. Complex seizures occur when the brain irritation spreads into the frontal and temporal lobes. In a generalized seizure, the irritation is spread over both sides of the brain; the patient may lose consciousness and his arms and legs will move uncontrollably. Loss of bladder and/or bowel control may occur (see Brainstorm: Managing a seizure).

These signs and symptoms may point to a brain tumor, but they’re not definitive. Let’s look next at ways to diagnose a brain tumor.

**Picture this**

Diagnosis begins with a thorough history. Ask the patient to describe his symptoms, calculate how long he’s had them, when they occur, whether he sees a connection to an activity or circumstance, and if they seem to be worsening.

A neurologic exam is the next order of business. This involves various tests of movement, vision, touch, hearing, smell, reflexes, eye response, balance and coordination, abstract thinking, mental status, and memory. Abnormal findings may be able to help pinpoint the area of the brain that’s affected.

Computed tomography (CT) scan is the most widely used diagnostic imaging test. Magnetic resonance imaging (MRI) is also used; it’s more sensitive for detecting intraparenchymal brain tumors like ependymomas, the most common brain tumor in children. Hemodynamic imaging combines CT scan or MRI with the ability to gauge the speed of contrast dye uptake; it’s useful for showing tumor neovascularization.

Cytologic studies of cerebrospinal fluid can be used to detect the presence of malignant cells shed by the tumor. An electroencephalogram can detect areas where abnormal brain waves occur and evaluate temporal lobe seizures. It can also be used to help rule out other disorders.

Once a lesion is pinpointed, a neurosurgeon will obtain a biopsy specimen via craniotomy to determine the histology or the tissue type of the tumor. Stereotactic (computer-directed) biopsy is an option when the lesion is too deep or in an area where craniotomy is too risky or when the patient can’t tolerate general anesthesia.

Next up: treatments.

**Reducing plan**

Whenever feasible, treatment for a brain tumor begins with surgery. The primary goal is to excise as much of the tumor as possible to reduce the severity of signs and symptoms while optimally preserving neurologic function (see Craniotomy: A hole in the head for postsurgical management). Let’s look at the other options that go along with surgery.
Radiation. Radiation therapy is useful for improving cure rates and prolonging survival for most types of primary brain tumors. The type of radiation technique used and the amount given depends on tumor histology, grade, and location and the patient’s physical status. Ionizing radiation targeting the tumor is delivered so as to minimize injury to the surrounding healthy tissue. The most common technique used is external beam radiation therapy. As the name implies, the radiation comes from a machine outside of the body. Treatment is generally given 5 days a week for 4 to 6 weeks for a total dose ranging from 40 to 70 Gy. Adverse effects may include hair loss, fatigue, nausea, vomiting, scalp dermatitis, and headache. Somnolence syndrome, characterized by mild drowsiness and fatigue to marked lethargy, is common after brain irradiation. It usually subsides 2 to 3 weeks after the start of therapy.

Stereotactic radiosurgery allows delivery of high-dose radiation in a single dose to a precise area in the brain. The goal of this technique is to eradicate the tumor cells within a targeted area and minimize damage to the surrounding tissues. Adverse effects may include headache. Also, the frame used to immobilize the patient’s head during this procedure may be uncomfortable.

Chemotherapy. Chemotherapy has been shown to boost survival in patients with gliomas, medulloblastomas, and certain other tumors. How well it works depends on the ability of the chemotherapeutic agent to cross the blood-brain barrier, a protective mechanism the body uses to stop potentially damaging substances from infiltrating the CNS. A few brain tumors actually serve to break down the barrier. Chemotherapy is generally used as adjuvant therapy to surgery and radiation. It can also be used for recurrent brain tumors.

Drug therapies. The combination of a corticosteroid like dexamethasone (Decadron), an osmotic diuretic like mannitol, and a loop diuretic like furosemide (Lasix) is used to reduce edema around the tumor. Otherwise, the swelling could cause brain structures to shift and increase ICP. The osmotic diuretic pulls fluid out of the space surrounding the tumor and

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**Match the treatment to the tumor type**

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Radiation/surgery</th>
<th>Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphomas</td>
<td>Whole-brain X-ray therapy</td>
<td>Intrathecal ethotrexate, procarbazine, vincristine, high-dose cytarabine</td>
</tr>
<tr>
<td>Medulloblastomas</td>
<td>Surgery, craniospinal radiation</td>
<td>Lomustine, cyclophosphamide, vincristine, cisplatin, etoposide</td>
</tr>
<tr>
<td>Gliomas</td>
<td>Surgery, radiation</td>
<td>Temozolomide, carmustine, procarbazine, carboplatin, irinotecan, etoposide</td>
</tr>
<tr>
<td>Astrocytomas</td>
<td>Surgery, radiation</td>
<td>Temozolomide, carmustine, procarbazine, carboplatin, irinotecan, etoposide</td>
</tr>
<tr>
<td>Oligodendrogliomas</td>
<td>Surgery, radiation</td>
<td>Procarbazine, lomustine, vincristine</td>
</tr>
<tr>
<td>Meningiomas</td>
<td>Surgery, external beam or stereotactic radiation</td>
<td>Hydroxyurea, alpha interferon</td>
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</tbody>
</table>
into the intravascular space, where the loop diuretic can push the kidney to excrete it. A steroid can also help to relieve headaches by lowering the ICP. Patients taking a steroid will need ulcer prophylaxis with a histamine-2-receptor blocker like famotidine (Pepcid) or a proton pump inhibitor like lansoprazole (Prevacid). Seizure medication may also be used. Aspirin and anticoagulation medications are stopped to avoid intracranial bleeds. Medications can be used in the nonspecific treatment of concentration and memory disturbances to manage coexisting depression, anxiety, or agitation. See Match the treatment to the tumor type and Plan B for more information.

Handling the tough jobs
A major part of your job is to help the patient manage his symptoms in a way that will best preserve his quality of life. Following are some guidelines for symptom management.

- Monitor headache onset, intensity, and symptoms. Advise the patient about medications, like steroids and analgesics, that will relieve the pain.

Plan B
Standard treatment sometimes falls short of improving the 5-year survival rate for certain tumor types. According to the National Cancer Institute, new biologic therapies being looked at include dendritic cell vaccination, tyrosine kinase receptor inhibitors, farnesyl transferase inhibitors, viral-based gene therapy, and oncolytic viruses. Patients with tumors that are unresectable or infrequently curable may benefit from radiosensitizers, hyperthermia, or interstitial brachytherapy used along with external beam radiation therapy to boost its benefit. Following are some of the other new treatment options in clinical trials.

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Standard treatment</th>
<th>Treatment options under study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pilocytic astrocytomas</td>
<td>Surgery or surgery and radiation</td>
<td>Nitrosourea-based chemotherapy, temozolomide</td>
</tr>
<tr>
<td>Anaplastic astrocytomas</td>
<td>Surgery plus radiation or surgery plus radiation and chemotherapy</td>
<td>Hyperfractionated irradiation, accelerated-fraction irradiation, stereotactic radiosurgery</td>
</tr>
<tr>
<td>Glioblastoma</td>
<td>Surgery plus radiation or surgery plus radiation and chemotherapy, carmustine (BCNU)-impregnated polymer (Gliadel wafer), radiation plus temozolomide</td>
<td>Hyperfractionated irradiation, accelerated-fraction irradiation, stereotactic radiosurgery</td>
</tr>
<tr>
<td>Oligodendrogial</td>
<td>Surgery or surgery plus radiation</td>
<td>Temozolomide, procarbazine-lomustine-vincristine (PCV) therapy</td>
</tr>
</tbody>
</table>

Monitor seizure activity and the type of seizure. Instruct the patient about appropriate antiseizure medications, including administration and adverse effects. See also Brainstorm: Managing a seizure.

The patient with a brain tumor may experience significant fatigue from the tumor.

Brainstorm: Managing a seizure

- Have the patient lie down immediately if he feels a seizure coming on. Some patients will have a warning symptom, like a visual aura or a smell.
- Loosen clothing around the neck and abdomen.
- Clear away all objects close to the patient that could injure him.
- Stay with the patient to provide support and to document manifestations of the seizure.
- Ensure airway patency. Never force a patient’s mouth open during a seizure.
- Once the seizure has subsided, provide reassurance and reorient the patient to time, place, and person.
itself or from the treatments. Advise him to get adequate rest, food, and fluids. Consult with a dietitian if nausea and vomiting or anorexia make it impossible for the patient to take in proper nutrition.

- The patient may experience cognitive impairment and/or memory loss. The provider may order medications that will reduce these distressing symptoms.

Providing plenty of good, understandable information so that the patient can make informed decisions about his care is one of the best ways you can help him cope with a diagnosis of brain tumor and its aftermath. “Is there anything you’d like to ask?” can be a key phrase in avoiding misapprehension. Often, you can use his questions as an indication of how much information he really wants to know.

Be on the lookout for symptoms of major depression in a long-term patient. Once the hectic back-and-forth of tests and chemo treatments disappears, the full implications of having a brain tumor may finally sink in and be overwhelming. Refer the patient and his family to hospital social services, which will provide them with information on the many brain tumor support groups available.

Learn more about it


Eating 3 square meals a day could be tough for your patient.