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GLIOBLASTOMA MULTIFORME; THE BRAIN TUMOUR

Dr. Dhrubo Jyoti Sen* and Pritha Halder

Department of Pharmaceutical Chemistry, School of Pharmacy, Techno India University, Salt-Lake City, Sector-V, EM-4, Kolkata-700091, West Bengal, India.

***Corresponding Author: Dr. Dhrubo Jyoti Sen**
Department of Pharmaceutical Chemistry, School of Pharmacy, Techno India University, Salt-Lake City, Sector-V, EM-4, Kolkata-700091, West Bengal, India.

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ABSTRACT
Brain tumors are common, requiring general medical providers to have a basic understanding of their diagnosis and management. The most prevalent brain tumors are intracranial metastases from systemic cancers, meningiomas, and gliomas, specifically, glioblastoma. Central nervous system metastases may occur anywhere along the neuroaxis, and require complex multidisciplinary care with neurosurgery, radiation oncology, and medical oncology. Meningiomas are tumors of the meninges, mostly benign and often managed by surgical resection, with radiation therapy and chemotherapy reserved for high-risk or refractory disease. Glioblastoma is the most common and aggressive malignant primary brain tumor, with a limited response to standard-of-care concurrent chemoradiation. The new classification of gliomas relies on molecular features, as well as histology, to arrive at an "integrated diagnosis" that better captures prognosis. This manuscript will review the most common brain tumors with an emphasis on their diagnosis, oncologic management, and management of medical complications.

KEYWORDS: Brain tumour, Cancer, tumour, Brain cancer.

Figure-1: Brain and Cancer.

INTRODUCTION

The possibility of being diagnosed with a brain tumor is a shocking and life-changing event. If your doctor suspects a brain tumor, it is important to seek out other doctors specialized in diagnosing and treating brain tumors.[1] The brain is a complex and vital organ, and treatment often causes life-long changes. It is important to get specialists' opinions and updated medical information about treatment options for the specific type of brain tumor.A brain tumor is a mass or growth of abnormal cells in your brain.[2] Many different types of brain tumors exist. Some brain tumors are noncancerous (benign), and some brain tumors are cancerous (malignant). Brain tumors can begin in your brain (primary brain tumors), or cancer can begin in other parts of your body and spread to your brain (secondary, or metastatic, brain tumors).[3] The growth rate as well as location of a brain tumor determines how it will affect the function of your nervous system. Brain tumor treatment options depend on the type of brain tumor you have, as well as its size and location.[4]

Major parts of brain

The brain has 3 main parts:

1. **Cerebrum.** This is the upper (supratentorial) part of the brain. It's composed of the right and left halves (hemispheres). Functions of the cerebrum include: language (spoken and written), initiation of movement, coordination of movement, processing of

vision and hearing, judgment, reasoning, problem solving, emotions, and learning.

2. **Cerebellum.** This is the lower (infratentorial) part of the brain. It's located at the back of the head, just above the neck. Its function is to coordinate voluntary muscle movements and to maintain posture, balance, and equilibrium.
3. **Brainstem.** The brainstem includes the midbrain, the pons, and the medulla. Functions of this area include: movement of the eyes and mouth, relaying sensory messages (hot, pain, loud, etc.), hunger, breathing, consciousness, cardiac function, body temperature, involuntary muscle movements, sneezing, coughing, vomiting, and swallowing.[5]

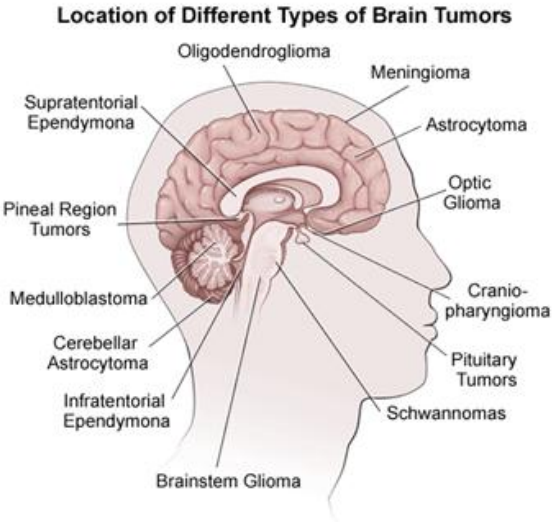


Figure-2: Brain anatomy.

MAJOR TYPES OF BRAIN TUMOUR

1. Primary tumor. This kind of tumor starts in the brain.

2. Secondary (metastatic) tumor. This kind of tumor is from a cancer that starts in another part of the body, then spreads to the brain.[6]

PRIMARY TUMOUR

- **Astrocytoma.** This kind of tumor comes from small star-shaped cells called astrocytes. In adults, an astrocytoma usually grows in the cerebrum. In children, they can grow in the cerebellum, cerebrum, and brain stem. Most astrocytoma spread into nearby normal brain tissue and are hard to cure with surgery. Glioblastoma is a type of astrocytoma that tends to grow very quickly.
- **Brain stem glioma.** This kind of tumor of the brain stem is more common in children than in adults. Because the brain stem controls many important functions, such as breathing and heart rate, this kind of tumor usually can't be removed by surgery.
- **Ependymoma.** This kind of tumor starts in cells that line the fluid-filled spaces within the brain (ventricles). It doesn't often grow into nearby brain tissue. This means in some cases it can be cured with surgery.
- **Oligodendroglioma.** This kind of tumor starts in cells that make myelin, the fatty substance that surrounds nerve cells. Like an astrocytoma, this tumor tends to spread into nearby brain tissue and is often hard to cure with surgery.[7]
- **Optic nerve glioma.** This kind of tumor grows in or around the nerve that sends messages from the eyes to the brain. This can cause vision changes. It can also cause hormone changes, due to its location near the pituitary gland.

Figure-3: Brain tumor.

Other types of primary tumors include:

- **Primitive Neuroectodermal Tumor (PNET).** This kind of tumor grows more often in children. It can grow anywhere in the brain in the primitive form of nerve cells. One type is the medulloblastoma. This kind of tumor is found in the cerebellum. They are more common in children than in adults. They tend to grow and spread quickly, but they can often be treated effectively.
- **Tumor of the pineal gland.** This kind of tumor grows in and around the pineal gland. This is a tiny organ near the center of the brain. The tumor can be slow-growing, called pineocytoma. Or it can be fast-growing, called pineoblastoma.[8]
- **Pituitary tumor.** This kind of tumor starts in the pituitary gland at the base of the brain. It is almost always benign. But it can cause serious symptoms because of its location, and because it may secrete excess hormones.
- **Craniopharyngioma.** This kind of tumor starts near the pituitary gland. It is usually slow growing. But it can cause symptoms if it presses on the pituitary gland or on nearby nerves.
- **Schwannoma.** This kind of tumor starts in myelin-making cells that surround certain nerves. It's most common in the vestibular nerve in the inner ear that helps with balance. If it grows there, the tumor is called a vestibular schwannoma or an acoustic neuroma. This type of tumor is usually benign.
- **Meningioma.** This kind of tumor starts in the outer linings of the brain (meninges). It is more common in adults. Many meningiomas can be removed with surgery, but some may grow back.
- **Primary central nervous system lymphoma.** This is an aggressive, rare type of tumor that starts in lymphocytes. This is a type of immune cell. The tumor is more common in people with a disease of

the immune system, such as AIDS. But it can grow in healthy people.[9]

SECONDARY TUMOUR

A secondary brain tumor is also known as a metastatic brain tumor. This is cancer that starts in another organ and then travels to the brain. In adults, secondary brain tumors are more common than primary brain tumors. Cancer in the brain that has spread from another part of the body is not considered brain cancer. It is still the same type of cancer as where it started. For example, lung cancer that has spread to the brain is called metastatic lung cancer. These are some of the most common types of cancer that spread to the brain:

1. Lung cancer 2. Breast cancer 3. Melanoma 4. Colon cancer 5. Kidney cancer

SYMPTOMS

Headaches are a common symptom of a brain tumor. You may experience headaches that:

1. Are worse in the morning when waking up
2. Occur while you're sleeping
3. Are made worse by coughing, sneezing, or exercise

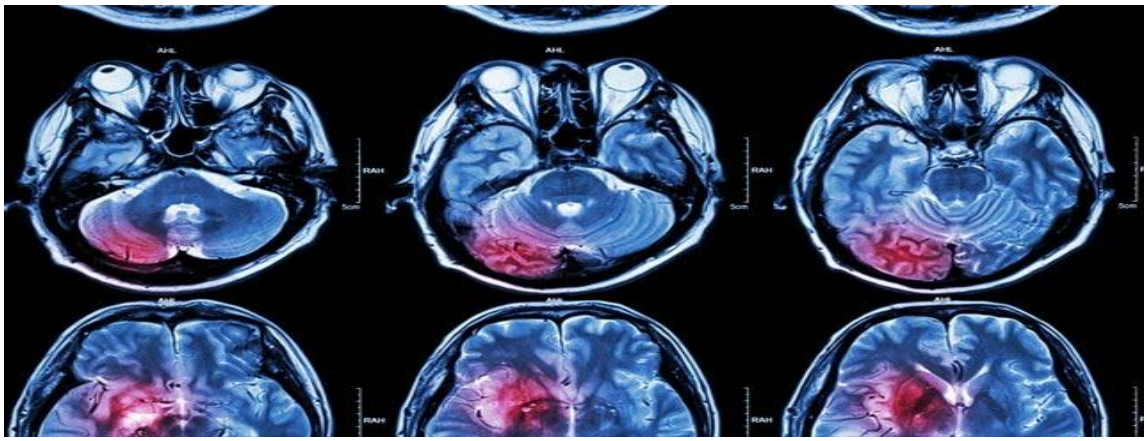


Figure-4: Computer Tomography of Brain Cancer.

1. Headache 2. Seizures 3. Personality or Memory Changes 4. Nausea or Vomiting 5. Fatigue 6. Drowsiness 7. Sleep Problem 8. Loss of balance 9. Anxiety or Depression 10. Mood swings 11. difficulty walking 12. muscle weakness in the face, arm, or leg 13. loss of balance 14. eye problems, such as drooping eyelids and unequal pupils.

RISK FACTOR

Family history- Only about 5-10% of all cancers are genetically inherited, or hereditary. It's rare for a brain tumor to be genetically inherited. Talk to your doctor if several people in your family have been diagnosed with a brain tumor.

Age-Risk for most types of brain tumors increases with age.

Race- Brain tumors in general are more common among Caucasians. However, African-American people are more likely to get meningiomas.[10]

Chemical exposure- Being exposed to certain chemicals, such as those you might find in a work environment, can increase your risk for brain cancer. Exposure to radiation People who have been exposed to ionizing radiation have an increased risk of brain tumors. You can be exposed to ionizing radiation through high-radiation cancer therapies. You can also be exposed to radiation from nuclear fallout. The nuclear power plant incidents in Fukushima and Chernobyl are examples of how people can be exposed to ionizing radiation.

No history of chicken pox- According tothe American Brain Tumor Association, people with a history of childhood chicken pox have a decreased risk of getting brain tumors.[11]

DIAGONOSIS OF BRAIN TUMOUR

Diagnosis of a brain tumor begins with a physical exam and a look at your medical history.Doctor will look inside your eyes with an ophthalmoscope, which is an instrument that shines a light through pupils and onto your retinas. This allows doctor to check how pupils react to light. It also allows doctor to look directly into eyes to see if there's any swelling of the optic nerve. When pressure increases inside the skull, changes in the optic nerve can occur.

The doctor may also evaluate your:

- Muscle strength
- Coordination
- Ability to do mathematical calculations
- Memory

CT scan of the head: CT scans are ways for your doctor get a more detailed scan of your body than they could with an X-ray machine. This can be done with or without contrast. Contrast is achieved in a CT scan of the head by using a special dye that helps doctors see some structures, like blood vessels, more clearly.[12]

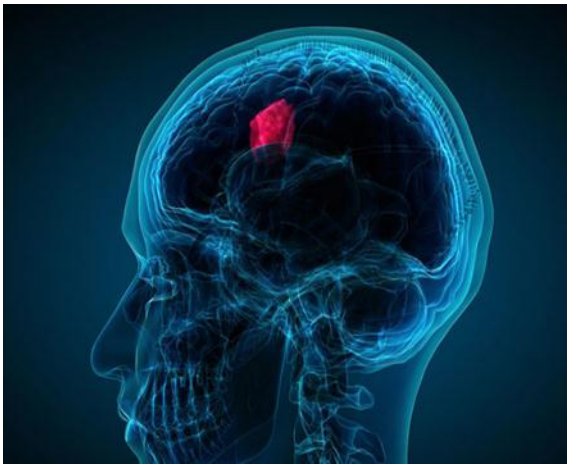


Figure-5: Brain MRI.

MRI of the head: If you have an MRI of your head, a special dye can be used to help your doctor detect tumors. An MRI is different from a CT scan because it doesn't use radiation, and it generally provides much more detailed pictures of the structures of the brain itself.

Angiography
This study uses a dye that's injected into your artery, usually in the groin area. The dye travels to the arteries in your brain. It allows your doctor to see what the blood supply of the tumors looks like. This information is useful at the time of surgery.

Skull X-rays: Brain tumors can cause breaks or fractures in the bones of the skull, and specific X-rays can show if this has occurred. These X-rays can also pick up calcium deposits, which are sometimes contained within a tumor. Calcium deposits may be in your bloodstream if your cancer has moved to your bones.[13]

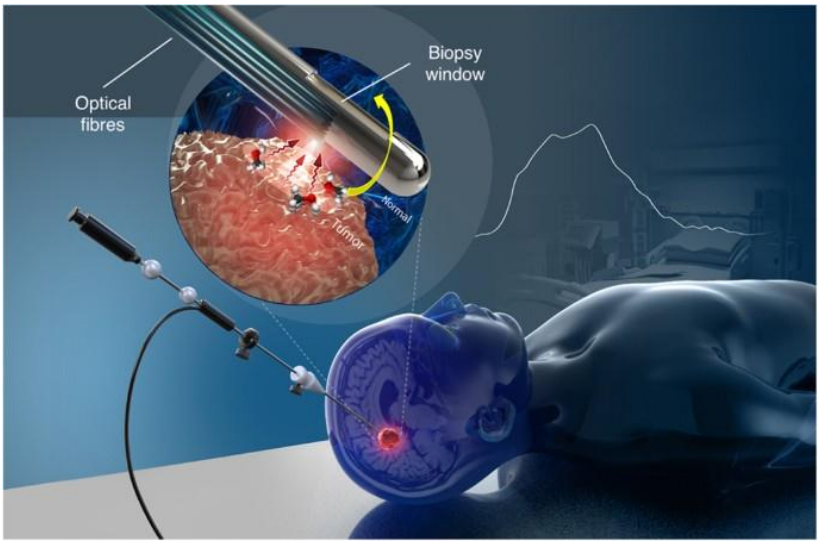


Figure-6: Brain biopsy.

Biopsy: A small piece of the tumor is obtained during a biopsy. A specialist called a neuropathologist will examine it. The biopsy will identify if the tumor cells are benign or malignant. It will also determine whether the cancer originated in your brain or another part of your body.

TREATMENT
The treatment of a brain tumor depends on:
1. The type of tumor
2. The size of the tumor
3. The location of the tumor
4. Your general health

Risks of brain surgery include infection and bleeding. Clinically dangerous benign tumors are also surgically removed. Metastatic brain tumors are treated according to guidelines for the type of original cancer.The most common treatment for malignant brain tumors is surgery. The goal is to remove as much of the cancer as possible without causing damage to the healthy parts of the brain. While the location of some tumors allows for easy and safe removal, other tumors may be located in an area that limits how much of the tumor can be removed. Even partial removal of brain cancer can be beneficial. Surgery can be combined with other treatments, such as radiation therapy and chemotherapy. Physical therapy,

occupational therapy, and speech therapy can help you to recover after neurosurgery.[14]

Brain Tumor Treatments

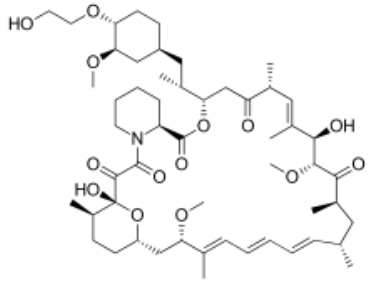
Surgery. **Surgery** is the usual treatment for most brain tumors. f the brain tumor is located in a place that makes it accessible for an operation, your surgeon will work to remove as much of the brain tumor as possible.

In some cases, tumors are small and easy to separate from surrounding brain tissue, which makes complete surgical removal possible. In other cases, tumors can't be separated from surrounding tissue or they're located near sensitive areas in your brain, making surgery risky. In these situations, your doctor removes as much of the tumor as is safe.

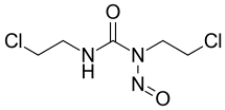
Even removing a portion of the brain tumor may help reduce your signs and symptoms.Surgery to remove a brain tumor carries risks, such as infection and bleeding. Other risks may depend on the part of your brain where your tumor is located. For instance, surgery on a tumor near nerves that connect to your eyes may carry a risk of vision loss.[15]

Radiation therapy. **Radiation therapy**, also called **radiotherapy**, is the use of high-powered rays to damage cancer cells and stop them from growing. Radiation therapy uses high-energy beams, such as X-rays or protons, to kill tumor cells. Radiation therapy can come from a machine outside your body (external beam radiation), or, in very rare cases, radiation can be placed inside your body close to your brain tumor (brachytherapy).External beam radiation can focus just on the area of your brain where the tumor is located, or it can be applied to your entire brain (whole-brain radiation). Whole-brain radiation is most often used to treat cancer that spreads to the brain from some other part of the body and forms multiple tumors in the brain.A newer form of radiation therapy using proton beams is being studied for use in people with brain tumors. For tumors that are very close to sensitive areas of the brain, proton therapy may reduce the risk of side effects associated with radiation. But proton therapy hasn't proved to be more effective than standard radiation therapy with X-rays.Side effects of radiation therapy depend on the type and dose of radiation you receive. Common side effects during or immediately following radiation include fatigue, headaches, memory loss and scalp irritation.[16]

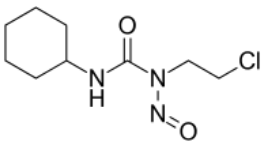
Drugs Approved for Brain Tumors



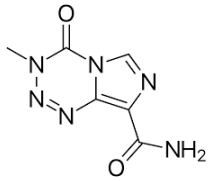
Afinitor (Everolimus)



BiCNU (Carmustine)



Lomustine



Temodar (Temozolomide)

Avastin (Bevacizumab): Monoclonal antibody

Chemotherapy. Chemotherapy uses drugs to kill tumor cells. Chemotherapy drugs can be taken orally in pill form or injected into a vein (intravenously). The chemotherapy drug used most often to treat brain tumors is temozolomide (Temodar), which is taken as a pill. Many other chemotherapy drugs are available and may be used depending on the type of cancer.Chemotherapy side effects depend on the type and dose of drugs you receive. Chemotherapy can cause nausea, vomiting and hair loss.Tests of your brain tumor cells can determine whether chemotherapy will be helpful for you. The type of brain tumor you have also is helpful in determining whether to recommend chemotherapy.[17]

CONCLUSION

Brain tumors can be cured completely by surgical excision, while for malignant **tumors** survival can be prolonged by chemo and radiotherapy after surgery. Early diagnosis and treatment is the keystone for **brain tumors.** The treatment of brain cancer is one of the most difficult challenges in neurosurgery and oncology. Malignant gliomas involve, in their progression, multiple aberrant signaling pathways and the BBB restricts the delivery of many chemotherapeutic agents. Targeted therapies have successfully been applied in cancers, but their efficacy remains low in malignant brain tumors. There are several factors underlying the disappointing results in brain cancer therapeutics including limited tumor cell drug uptake, intracellular drug metabolism, inherent tumor sensitivity to chemotherapy, and cellular mechanisms of resistance. The results in the first experimental studies suggest that a single antiangiogenic therapy is not sufficient to eradicate glioma.

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