



REVIEW ON ASSESSING THE RISK OF BRAIN TUMORS IN YOUNG POPULATION

K. Malleswari^{*1}, Dr. D. Rama Bramha Reddy^{*2}, O. Venkata Nandini^{*3}, P. Aswini^{*4} and P. Taskeen^{*5}

^{*1}Associate Professor, Pharmaceutics, Nalanda Institute of Pharmaceutical Sciences, Sattenapalli, Kantepudi, Andhra Pradesh, India.

^{*2}Principal, Phytochemistry, Pharmaceutical Sciences, Sattenapalli, Kantepudi, Andhra Pradesh, India.

^{*3,4,5}Student, B. Pharmacy, Nalanda Institute of Pharmaceutical Sciences, Sattenapalli, Kantepudi, Andhra Pradesh India.



***Corresponding Author: K. Malleswari**

Associate Professor, Pharmaceutics, Nalanda Institute of Pharmaceutical Sciences, Sattenapalli, Kantepudi, Andhra Pradesh, India. Email ID:

Article Received on 15/05/2024

Article Revised on 05/06/2025

Article Accepted on 25/06/2025

ABSTRACT

Primary brain tumors account for ~1% of new cancer cases and ~2% of cancer deaths in the United States; however, they are the most commonly occurring solid tumors in children. These tumors are very heterogeneous and can be broadly classified into malignant and benign (or non-malignant), and specific histologies vary in frequency by age, sex, and race/ethnicity. Epidemiological studies have explored numerous potential risk factors, and thus far the only validated associations for brain tumors are ionizing radiation (which increases risk in both adults and children) and history of allergies (which decreases risk in adults). Studies of genetic risk factors have identified 32 germline variants associated with increased risk for these tumors in adults (25 in glioma, 2 in meningioma, 3 in pituitary adenoma, and 2 in primary CNS lymphoma), and further studies are currently under way for other histologic subtypes, as well as for various childhood brain tumors. While identifying risk factors for these tumors is difficult due to their rarity, many existing datasets can be leveraged for future discoveries in multi-institutional collaborations. Many institutions are continuing to develop large clinical databases including pre-diagnostic risk factor data, and developments in molecular characterization of tumor subtypes continue to allow for investigation of more refined phenotypes.

KEYWORDS: Epidemiology, glioma, meningioma, pediatric brain tumors, risk factors.

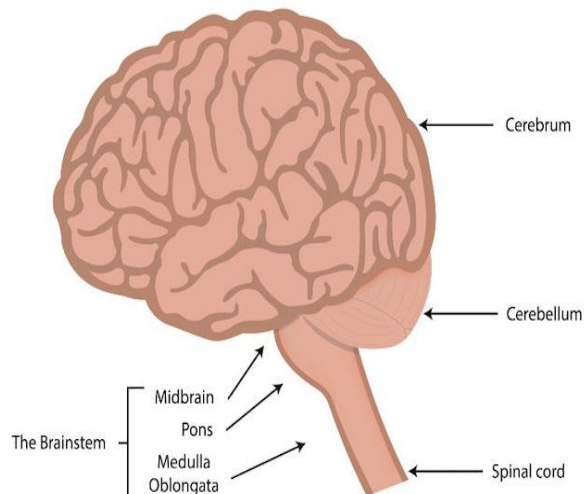
INTRODUCTION

The human brain, which serves as the control center for all the body's organs, is a highly developed organ that enables a person to adapt to and withstand various environmental situations.^[1] The human brain allows people to express themselves in words, carry out activities, and express thoughts and feelings. Cerebrospinal fluid (CSF), white matter (WM), and gray matter (GM) are the three major tissue components of the human brain. The gray matter regulates brain activity and comprises neurons and glial cells. The cerebral cortex is connected to other brain areas through white matter fibers comprising several myelinated axons. The corpus callosum, a substantial band of white matter fibers, connects the left and right hemispheres of the brain.^[2] A brain tumor is a brain cell growth that is out of control and aberrant. Any unanticipated development may affect human functioning since the human skull is a rigid and volume-restricted structure, depending on the area of the brain involved. Additionally, it might spread to other organs, further jeopardizing human functions.^[3] Early

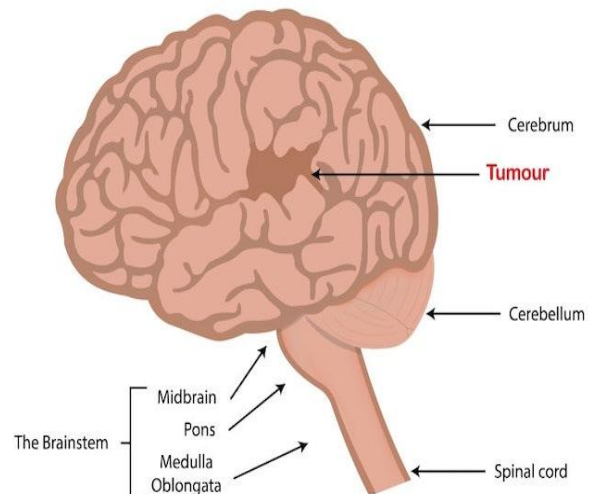
cancer detection makes the ability to plan effective treatment possible, which is crucial for the healthcare sector.^[4] Cancer is difficult to cure, and the odds of survival are significantly reduced if it spreads to nearby cells. Undoubtedly, many lives could be preserved if cancer was detected at its earliest stage using quick and affordable diagnostic methods. Both invasive and noninvasive approaches may be utilized to diagnose brain cancer. An incision is made during a biopsy to extract a lesion sample for analysis. It is regarded as the gold standard for the diagnosis of cancer, where pathologists examine several cell characteristics of the tumor specimen under a microscope to verify the malignancy.^[1]

Brain Tumour

Healthy Brain



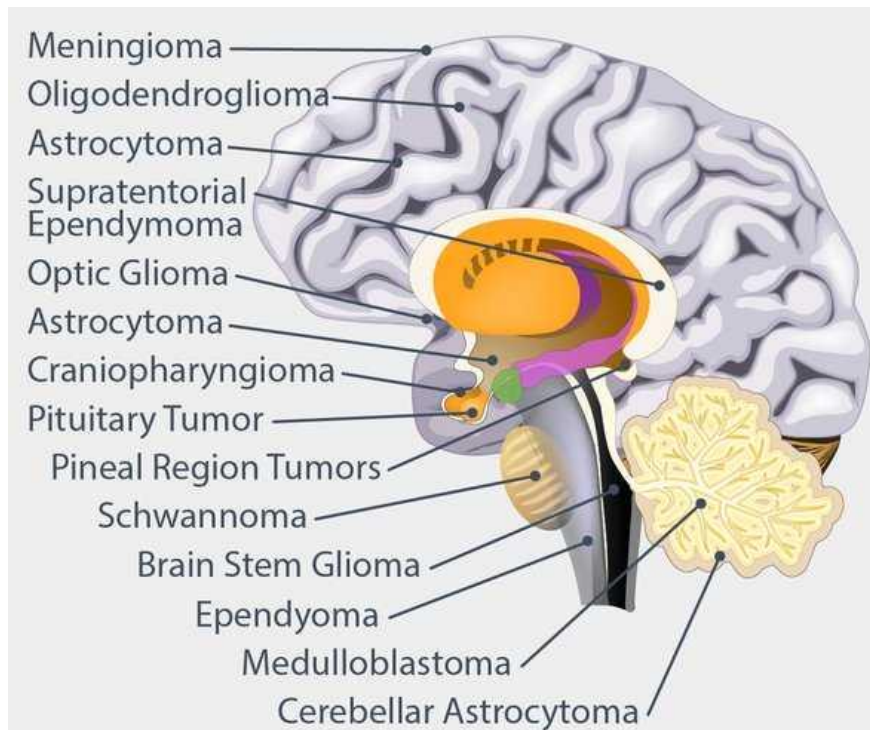
Brain with a Tumour



Brain Tumor

A brain tumor can form in the brain cells it can begin elsewhere and spread to the brain. As the tumor grows, it creates pressure on and changes the function of

surrounding brain tissue, which causes signs and symptoms such as headaches, nausea and balance problem.



Types of brain tumors

The main three parts of the brain are the brain stem, cerebrum, and cerebellum. The cerebellum is the second-largest component of the brain and manages bodily motor activities, including balance, posture, walking, and

general coordination of movements. It is positioned behind the brain and connected to the brain stem.^[2] Internal white matter, tiny but deeply positioned volumes of gray matter, and a very thin gray matter outer cortex can all be found in the cerebellum and cerebrum. The

brainstem links to the spinal cord. It is situated at the brain's base. Vital bodily processes, including motor, sensory, cardiac, repositories, and reflexes, are all under the control of the brainstem. Its three structural components are the medulla oblongata, pons, and midbrain. A brain tumor is the medical term for an unexpected growth of brain cells. According to the tumor's location, the kind of tissue involved, and whether they are malignant or benign, scientists have categorized several types of brain tumors based on the location of the origin (primary or secondary) and additional contributing elements. The World Health Organization (WHO) categorized brain tumors into 120 kinds. This categorization is based on the cell's origin

and behavior, ranging from less aggressive to greater aggressive. Even certain tumor forms are rated, with grades I being the least malignant (e.g., meningiomas, pituitary tumors) and IV being the most malignant. Despite differences in grading systems that rely on the kind of tumor, this denotes the pace of growth.^[3] The most frequent type of brain tumor in adults is glioma, which may be classified into HGG and LGG. The WHO further categorized LGG into I–II grade tumors and HGG into III–IV grade. To reduce diagnosing errors, accurate identification of the specific type of brain disorder is crucial for treatment planning. A summary of various types of brain tumors is provided in.

Table 1: Types of brain tumors.

Types of Tumors Based on	Type	Comment
Nature	Benign	Less aggressive and grows slowly
	Malignant	Life-threatening and rapidly expanding
Origin	Primary tumor	Originates in the brain directly
	Secondary tumor	This tumor develops in another area of the body like lung and breast before migrating to the brain

Meningioma

meningioma is the most common primary brain tumor, accounting for more than 30% of all brain tumors. Meningiomas originate in the meninges, the outer three layers of tissue that cover and protect the brain just under the skull. Women are diagnosed with meningiomas more often than men. About 85% of meningiomas are noncancerous, slow-growing tumors. Almost all meningiomas are considered benign, but some meningiomas can be persistent and come back after treatment.

Pituitary Adenoma

Adenoma, a type of tumor that grows in the gland tissues, is the most common type of pituitary tumor. Pituitary adenomas develop from the pituitary gland and tend to grow at a slow rate. About 10% of primary brain tumors are diagnosed as adenomas. They can cause vision and endocrinological problems. Fortunately for patients affected by them, adenomas are benign and treatable with surgery and/or medication.

Craniopharyngioma

These benign tumors grow near the pituitary gland and can appear as solid tumors or cysts. Craniopharyngiomas often press on nerves, blood vessels or parts of the brain around the pituitary gland. Like adenomas, they can also cause vision and endocrinological issues. They usually affect children and teens as well as adults over the age of 50.

Schwannomas

are benign, slow-growing tumors of the nerve that connects the ear to the brain. Less than 8% of primary brain tumors are acoustic neuromas. They usually develop in middle-aged adults, grow on the nerve sheath

— the covering surrounding the nerve fibers — and often cause hearing loss. Schwannomas can also affect the trigeminal nerve. These are called trigeminal schwannomas, which are much less common than vestibular schwannomas and can cause facial pain.

Nasopharyngeal Angiofibroma

Nasopharyngeal angiofibroma, also known as juvenile nasopharyngeal angiofibroma, is a benign skull base tumor in the nose that is usually diagnosed in adolescent boys. It is the most common benign tumor of the nasopharynx (the space at the back of the nose that connects the nose with the mouth). It spreads to areas around the nose, causing symptoms such as congestion and nosebleeds.

Neurofibroma

Neurofibromas are benign, generally painless tumors that can grow on nerves anywhere in the body. In some cases, these soft, fleshy growths develop in the brain, on cranial nerves or on the spinal cord. Multiple neurofibromas are a symptom of a genetic disorder.

Hemangioblastoma

Hemangioblastomas are benign tumors of the blood vessels that can form in the brain. These tumors can often be removed through surgery. In rare occasions, they can appear in multiple sites and be symptomatic of a hereditary disease called . If that is the case, different tests and visits with a specialist such as an ophthalmologist or geneticist may be recommended.

Chondroma

Chondromas are very rare benign tumors made of cartilage. They can develop in the cartilage found in the skull base and the paranasal sinuses, but they can also

affect other body parts such as the hands and feet. Chondromas typically occur in patients between the ages of 10 and 30. While these tumors grow slowly, they may eventually cause the bone to fracture or grow too much, creating pressure on the brain.

Osteoma

Osteomas are benign bone tumors (new bone growth) that usually develop on the skull base and facial bones.

Differences between Benign tumor& malignant tumor

Benign Tumour	Malignant Tumour
1. It is non-cancerous tumour.	1. It is cancerous tumour.
2. Benign tumour stops growth after reaching a certain size.	2. Malignant tumour shows indefinite growth.
3. It gets covered over by a capsule of connective tissue.	3. Encapsulation is absent.
4. Benign tumour is non-invasive.	4. It shows metastasis by invading other parts of the body.
5. Limited adherence occurs amongst cells of benign tumour.	5. There is no adherence amongst cells. They tend to slip past one another.
6. There is no latent period.	6. A latent period occurs between initiation and progression of tumour.
7. Growth is slow.	7. Once started, growth of tumour is rapid.
8. It causes very little damage.	8. It causes fatal damage to the body.

Epidemiology and pathogens

The exact pathophysiology of BTRE is not well characterized; however, it is thought to be multifactorial (Tumor burden, type, location, growth rate, microenvironment of the blood-brain barrier, altered neurotransmitter homeostasis, and gap junction alterations are factors that influence BTRE. The likelihood of epilepsy among patients with brain tumors differs depending on the tumor's histopathological subtype. Patients with low-grade gliomas have a greater tendency to suffer from seizures than those with high-grade gliomas. One study found that patients diagnosed

with low-grade glioma had a significantly higher rate of seizures compared to patients diagnosed with glioblastoma (85% vs. 49%, respectively). Dysembryoplastic neuroepithelial tumors (DNETs) and gangliogliomas have an extremely high propensity for seizures with an incidence greater than 80%. Metastatic lesions tend to have a low incidence of seizures (Melanoma, however, has the highest seizure rate among the metastatic lesions because it involves gray matter, frequently has multiple lesions, and has an intrinsic high frequency of hemorrhage.^[5]

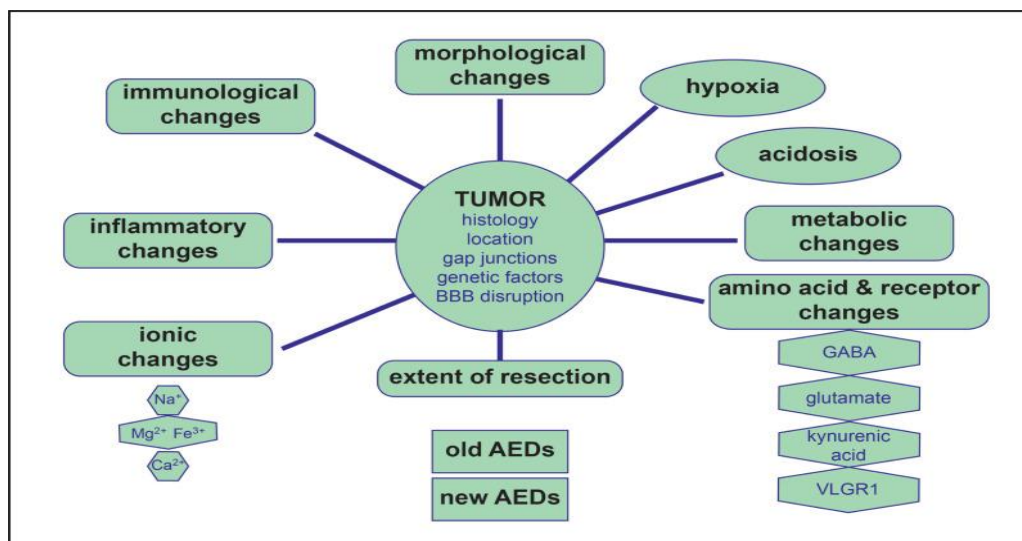


Table 1: Seizures by tumor location in 65 patients with gliomas.

Tumor Location	Seizure at Onset	Recurrent Seizures	Late Onset Seizures	Status Epilepticus
Frontal	10/19	8/10	2/9	0/19
Temporal	3/11	3/3	2/8	1/11
Parietal	10/24	7/10	3/14	5/24
Occipital	0/2	–	2/2	1/2
Multifocal/Bilateral	6/9	3/6	1/3	3/9

Tumor growth rate

Studies show that seizure prevalence and tumor growth rate are inversely proportional. Intuitively, slower growing and more indolent gliomas have a longer amount of time to provoke a seizure. Moreover, epileptogenesis requires complex re-organization and vascularization of tumor cells which often does not happen with rapidly growing tumors (Moreover, slow growing neoplasms tend to possess innate epileptogenic properties.^[6]

The pathogenesis of epilepsy differs among the various types of tumors. Tumors such as DNETs have high incidence of seizure because they tend to cause cortical disruption due to disruption of the underlying cortical and subcortical structures. The mechanisms behind the higher seizure frequency of other low-grade lesions is likely secondary to mechanical and vascular changes which slowly develop overtime. In contrast, high-grade gliomas and other rapidly dividing tumors tend to cause seizures because of irritation from necrosis or products of hemorrhage, such as hemosiderin.

Treatment

Treatment options vary depending on the type, grade, size and location of the tumor; whether it has spread; and your age and general health. The goal of treatment may be curative or focus on relieving symptoms (palliative care). Treatments are often used in combination with one another. The goal is to remove all or as much of the tumor as possible through surgery to minimize the chance of recurrence. Radiation therapy and chemotherapy are used to treat tumors.^[7]

Surgery

Surgery is the treatment of choice for brain tumors that can be reached without causing major injury to vital parts of the brain. Surgery can help to refine the diagnosis, remove as much of the tumor as possible, and release pressure within the skull. A partial removal can still relieve symptoms. Radiation or chemotherapy may be used on the remaining tumor cells. Improvements in techniques, particularly imageguided surgery, intraoperative MRI/CT, and functional brain mapping have improved the surgeon's ability to precisely locate the tumor, define the tumor's borders, avoid injury to vital brain areas, and confirm the amount of tumor removal while in the operating room.

Radiation

Radiation therapy uses controlled high-energy rays to treat brain tumors. Radiation works by damaging the

DNA inside cells making them unable to divide and reproduce. The goal of radiation therapy is to maximize the dose to abnormal cells and minimize exposure to normal cells. The benefits of radiation are not immediate but occur over time. Aggressive tumors, whose cells divide rapidly, typically respond more quickly to radiation. There are two ways to deliver radiation, external and internal.

- Stereotactic radiosurgery (SRS) delivers a high dose of radiation during a single session. Although it is called surgery, no incision is made.
- Fractionated stereotactic radiotherapy (FSR) delivers lower doses of radiation over many visits.

Chemotherapy

Chemotherapy drugs work by interrupting cell division. However, it affects not only tumor cells but normal cells, thus causing side effects, especially in fast growing cells (e.g., hair, digestive, blood). Treatment is delivered in cycles with rest periods in between to allow the body to rebuild healthy cells. Chemotherapy drugs can be administered orally as a pill, intravenously (IV), or as a wafer placed surgically into the tumor. The drugs most commonly used to treat brain tumors are carmustine (BCNU), lomustine (CCNU), and temozolomide (Temodar). Chemotherapy is also used as a radio-sensitizing agent that increases tumor cell death during radiation therapy. Agents that often work in high-grade gliomas include procarbazine, platinum analogs (cisplatin, carboplatin), the nitrosureas (BCNU, CCNU), and alkylating agents (temozolomide, vincristine). BCNU has been proven effective when applied locally to the tumor bed after the tumor has been removed. By applying it directly to the diseased area of the brain, side effects are limited and the drug has a more beneficial effect.

Diagnosis

Clinical signs and symptoms of primary brain tumors may be general or focal. General symptoms, such as headache and seizures, are due to increased intracranial pressure.⁸ Focal symptoms, such as unilateral weakness or personality changes, are due to tissue destruction or compression of specialized regions.⁹ Initial symptoms of low-grade tumors or initial stages of disease are often focal, progressing to generalized symptoms as the tumor increases in size and spreads.^{10,11} The following have been reported by patients as the first symptom of a primary brain tumor: headache (23.5% of patients); generalized seizures (21.3%); unilateral weakness (7.1%); unsteadiness (6.1%); expressive language disorder (5.8%); visual problems (3.2%); confusion

(4.5%); unilateral numbness (2.3%); personality problems (1.6%); diplopia (0.3%); and other symptoms (24.2%), such as anosmia, apraxia, cognitive delay, drowsiness, dysphagia, hallucinations, memory loss, nausea and vomiting, pain, and stiff neck.^[8]

Magnetic resonance imaging (MRI): An MRI creates a series of detailed pictures of your brain and spinal cord using a magnet, radio waves, and a computer. It may be performed with or without a contrast medium called gadolinium. If a contrast medium is used, you will receive an injection before your scan. The injected substance is used to highlight cancer cells in the pictures.

Computed tomography (CT) scan: A CT scan uses a computer linked to an X-ray machine. It produces a

series of detailed pictures of areas inside your brain taken from different angles. A dye may be swallowed or injected into your vein to help tissues or organs show up better in the pictures.

Positron-emission tomography (PET) scan: A PET SCAN involves the injection of a small amount of radioactive glucose into your vein. The PET scanner rotates around your body and produces a picture of where glucose is being used in your brain. Malignant tumor cells appear brighter in the images because they absorb more glucose. A PET scan can differentiate between a growing tumor and inflammation.^[9]

Symptoms



CONCLUSIONS

There is an indisputable increase in safety achieved through the combination of monitoring and mapping techniques. If they are easily and quickly available, these techniques should be aimed for in brain tumour surgeries as described in this paper as a standard procedure. However, we have showed that, deviating from the established combined technical setup of monitoring and mapping possibilities, using a mapping-only device, can achieve comparable results in terms of postoperative deficits and resection outcomes. We have demonstrated that a mapping only technique is safe (2% deficit) and efficient. Brain tumour surgery is performed in many countries around the world. With the help of a mapping-only technique, eloquently located tumors can be treated with great safety and very good resection results. This is a prerequisite for improved outcomes after therapy for aggressive diseases, not least in the case of high-grade

infiltrative tumors. Given the simple logistics needed and the affordable price of the technology, we hope that our report promotes the supply and availability of mapping only devices in neurosurgical units under careful consideration of special indications. We think that this could be an absolute gain for brain tumour patients, especially in the field of emergency care, or in health care systems where there might be limited financial—and therefore personnel and technical—access to functional monitoring resources for patients with eloquent brain tumors.

REFERENCES

1. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, Ohgaki H, Wiestler OD, Kleihues P, Ellison DW. The 2016 World Health Organization classification of tumors

of the central nervous system: a summary. *Acta neuropathologica*, 194-235.

2. Jellinger K.A The Human Nervous System Structure and Function, 6th edn, 16: 1468-1331.
3. Johnson D. R., Guerin J. B., Giannini C., Morris J. M., Eckel L. J., Kayfmann T. J., Update to the WHO Brain Tumor Classification System:What the radiologist Needs to Know. *Radiographics*, 37: 2164-2180.
4. Bunkner J. C., Brown P. D., O' Neill B. P., Meyer F. B., Wetmore C. J., Uhm J. H. Central Nervous system Tumors. *Mayo Clinic*, 82: 1271-1386.
5. Chen DY, Chen CC, Crawford JR, Wang SG tumor-related epilepsy:epidemiology, Pathogenesis and management. *J Neurological*, 13-21.
6. Killinger NV, Shah AK, Mittal S. Management of brain tumor-related epilepsy. *Neurol India*, 35-68.
7. Carrie A M, Timothy F C. Brain tumor treatment: chemotherapy and other new developments. *Seminars in Oncology Nursing*, 260-272.
8. Newton HB. Primary brain tumors: review of etiology, diagnosis and treatment. *Am Fam Physician*, 787-797.
9. Laws ER, Parney IF, Huang W, et al.; Glioma Outcomes Investigators. Survival following surgery and prognostic factors for recently diagnosed malignant glioma. *J Neurosurg*, 467-473.