

## A COMPREHENSIVE REVIEW ON BRAIN TUMOR

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### ABSTRACT

Brain tumors are intracranial lesions that occupy space in the skull. Brain tumors are relatively rare but deadly cancers, and present challenges in the determination of risk factors in the population. These tumors are inherently difficult to cure because of their protected location in the brain, with surgery, radiation and chemotherapy options carrying potentially lasting morbidity for patients and incomplete cure of the tumor. Brain tumors are life threatening because the space inside the skull is limited, their growth increases intracranial pressure, and may cause edema, reduced blood flow, and displacement, with consequent degeneration, of healthy tissue that controls vital functions. Brain tumors are, in fact, the second leading cause of cancer related deaths in children and young adults. The development of methods to prevent or detect brain tumors at an early stage is extremely important to reduce damage to the brain from the tumor and the therapy. Developing effective prevention or early detection methods requires a deep understanding of the risk factors for brain tumors.

**Keywords:** Brain tumors, surgery radiation therapy, risk factors, metastasis.

### INTRODUCTION

A tumor also called as neoplasm or lesion is abnormal tissue that grows by uncontrolled cell division. Normal cells grow in a controlled manner as new cells replace old or damaged cells. For reasons not fully understood, tumor cells reproduce uncontrollably.

Brain tumour is an abnormal growth occurring in any tissue contained within the cranium, including the brain, cranial nerves, meninges, skull, pituitary gland, and pineal gland. Brain tumors are named after the cell type from which they grow. They may be primary (starting in the brain) or secondary (spreading to the brain from other area). Treatment options vary depending on the tumor type, size and location; whether the tumor has spread; and the age and medical health of the person. Treatment options may be curative or focus on relieving symptoms. Of the more than 120 types of brain tumors, many can be successfully treated. New therapies are improving the life span and quality of life for many people.

Primary brain tumors do not spread to other body sites, and can be malignant or benign. Secondary brain tumors are always malignant. Both types are potentially disabling and life threatening<sup>1</sup>.

A benign brain tumor grows slowly has distinct boundaries, and rarely spreads. Although its cells are not malignant, this tumor composed of benign cells and located in vital areas can be considered as life threatening.

A malignant brain tumor grows quickly has irregular boundaries and spreads to nearby brain areas. Although they are sometimes called brain cancer, malignant brain tumors do not fit the definition of cancer because they do not spread to organs outside the brain and spinal cord. Malignant brain tumors are comprised of a number of different malignancies, including gliomas, medulloblastomas, primary central nervous system (CNS) lymphomas, and brain metastases. There are a number of distinct types of brain cancers within the brain, and the treatments and their outcomes vary greatly based on pathologic and histologic diagnosis. More recently,

researchers are identifying new therapies based on increased knowledge of cellular and molecular biology<sup>2</sup>.

Metastatic (secondary) brain tumors begin as cancer elsewhere in the body and spread to the brain. They form when cancer cells are carried in the blood stream to the brain. The most common cancers had spread to the brain are lungs and breast.

### Types of Primary Brain Tumors

There are many types of primary brain tumors. Primary brain tumors are named according to the type

of cells or the part of the brain in which they begin. For example, most primary brain tumors begin in glial

cells. This type of tumor is called a *glioma*.

Among adults, the most common types are:

- **Astrocytoma:** The tumor arises from star-shaped glial cells called *astrocytes*. It can be any grade. In

adults, an astrocytoma most often arises in the cerebrum.

- **Grade I or II astrocytoma:** It may be called a low-grade glioma.
- **Grade III astrocytoma:** It's sometimes called a high-grade or an anaplastic astrocytoma.
- **Grade IV astrocytoma:** It may be called a *glioblastoma* or malignant astrocytic glioma.

- **Meningioma:** The tumor arises in the meninges. It can be grade I, II, or III. It's usually benign (grade I) and grows slowly.

- **Oligodendroglioma:** The tumor arises from cells that make the fatty substance that covers and protects nerves. It usually occurs in the cerebrum. It's most common in middle-aged adults. It can be grade II or III.

Among children, the most common types are:

- **Medulloblastoma:** The tumor usually arises in the cerebellum. It's sometimes called a *primitive neuroectodermal tumor*. It is grade IV.

- **Astrocytoma:** It is mainly **Grade I or II** In children, this low grade tumor occurs anywhere in the brain. The most common astrocytoma among children is *juvenile pilocytic astrocytoma*. It's grade I.

- **Ependymoma:** The tumor arises from cells that line the ventricles or the central canal of the spinal cord. It's most commonly found in children and young adults. It can be grade I, II, or III.

- **Brain stem glioma:** The tumor occurs in the lowest part of the brain. It can be a low-grade or high-grade tumor. The most common type is *diffuse intrinsic pontine glioma*.

### Grading System

Brain tumors are graded from I to IV.

Grade	Characteristics
I	Slow growing cells Almost normal appearance Least malignant Usually associated with long-term survival
II	Relatively slow growing cells Slightly abnormal appearance Can invade nearby tissue Sometimes recur as a higher grade
III	Actively reproducing abnormal cells Abnormal appearance Infiltrate normal tissue Tend to recur, often as a higher grade
IV	Rapidly reproducing abnormal cells Very abnormal appearance Area of dead cells (necrosis) in center Form new blood vessels to maintain growth <sup>3,4</sup>

### Causes

The main causes of tumors like brain tumors are not known. From different studies it has been found that people most at risk for brain tumors include those who have:

- cancer elsewhere in the body
- prolonged exposure to pesticides, industrial solvents, and other ionizing radiations.
- inherited diseases, such as neurofibromatosis.
- environmental factors are also responsible.<sup>5</sup>

### Symptoms

The most common symptoms at the time of diagnosis include headache, nausea and vomiting, cognitive impairment. Headaches are probably the most common symptom. Patterns that may occur with brain tumors include:

- Headaches that get worse when waking up in the morning, and then go away within a few hours

- Headaches that get worse with coughing or exercise, or with a change in body position
- Headaches that occur while sleeping and with at least one other symptom (such as vomiting or confusion)

Patients with brain tumors may have a seizure. This may be the first symptom or sign.

Sometimes the only symptoms of brain tumors are mental changes, which may include:

- Changes in personality and behaviour
- Impaired concentration
- Increased sleep
- Memory loss
- Problems with reasoning

Other possible symptoms are:

- Gradual loss of movement or feeling in an arm or leg
- Hearing loss, with or without dizziness
- Speech difficulty
- Unexpected vision problem, including vision loss in one or both eyes, or double vision
- Unsteadiness and problems with balance
- Weakness or numbness

Symptoms of a brain tumour depend on several factors including the size of the tumour, its location in the brain, and how rapidly it is growing.

According to tumor location:

#### 1. Frontal lobe

Mental disorder / mild personality disorders: depression, confusion, bizarre behavior, it is difficult to give an argument / judge true or not, hemiparesis, ataxia, and slurred speech.

#### 2. Presentalis posterior cortical

Weakness / paralysis of the facial muscles, tongue and fingers

#### 3. Lobes parasentralis

Weakness in the lower extremities

#### 4. Occipital lobe

Seizures, impaired vision

#### 5. Temporal lobe

Tinnitus, auditory hallucinations, sensory aphasia, paralysis of facial muscles

#### 6. Parietal lobe

Lost sensory function, kortikalis, localization sensory disturbances, visual disturbances

#### 7. Cerebrulum

Papil edema, headache, motor disorders, hypotonia, joint hiperekstremite.6

### Risk factors

The cause of brain cancer is still largely unknown. Although there are some genetic conditions and environmental factors which may contribute to the development of brain cancer, the risk factors are much less defined for brain cancer than for other cancers in the body.

Also, the risk of developing primary brain cancer is very low. The American Cancer Society estimates the risk over a lifetime is less than one percent.

It's important to remember that a brain cancer risk factor only affects the probability of developing brain cancer over a lifetime.

### GENERAL

- **Gender:** There is no general rule that covers all brain cancers. Certain cancers, like meningiomas, are twice as likely to develop in women. Medulloblastomas are more frequently found in males.
- **Age:** In general, the frequency of brain cancer increases with age, with more occurrences in individuals age 65 and older. The age factor varies depending on the cell type and location of common in adults. The incidence of meningiomas and craniopharyngiomas are far more frequent in adults over age 50, but again, these tumors may occur at any age.

### BODY

- **Compromised immune system:** Some people with compromised immune systems have an increased risk of developing lymphomas of the brain.

### GENETICS

- **Genetic links:** Family history may affect the likelihood of developing certain diseases. Von Hippel-Lindau disease, Li-Fraumeni syndrome, and Neurofibromatosis (NF1 and NF2) are inherited conditions that have been found in families with a history of rare brain tumors. Otherwise, there is little evidence that brain cancer runs in families.

### EXPOSURES

- **Chemical exposure:** Exposure to certain industrial chemicals or solvents has been linked to an increased risk in developing brain cancer. Although it is not conclusive, there is evidence that there is

a higher incidence of certain types of brain tumors in individuals who work in oil refining, rubber manufacturing and drug manufacturing.<sup>7</sup>

### Pathophysiology

More recent studies have focused on molecular pathobiology and pathophysiology that underlie these lesions and differentiate them from normal tissue Brain tumor causing neurological disorders. The symptoms occur sequentially.

Neurologic symptoms in brain tumors typically considered to be caused by two factors focal disruption, caused by the tumor and intracranial pressure.

Changes in blood supply caused by the pressure of growing tumors causing brain tissue necrosis. Seizures as a manifestation of neuro sensitivity changes associated with invasion and compression changes in blood supply to the brain tissue. Some cysts also form tumors suppress the surrounding brain parenchyma thus aggravate focal neurological disorders.

Increased intracranial pressure can be caused by several factors: the increase of mass in the skull, edema formation around the tumor and cerebrospinal circulation changes. Mass resulting in increased tumor growth, because tumors will take the space of a relatively rigid skull.

Malignant tumors cause edema in brain tissue. Seluruhnyanya yet understood mechanism, but due to the difference in osmotic allegedly causing bleeding. Venous obstruction and edema caused by damage to the blood brain barrier, all cause an increase in intracranial volume.

Compensation mechanism requires many days / months to be effective and enumerated as useless ity arises when the intracranial pressure quickly. This compensation mechanism among other works to lower intracranial blood volume, cerebrospinal fluid volume, intracellular fluid content and reduce parenchymal cells. The increase in pressure resulting in untreated ulcer or serebulum herniation. Herniation occurs when the medial lobe gyrus temporals shifted to inferior through tentorial notch by a mass in the brain hemispheres. Herniation pressing ensefalon men menyebabkan loss of consciousness and neurological menekan third. At serebulum herniation, tonsillar before shifting down through the foramen magnum by a posterior mass. Compression of the medulla oblongata and stopping breathing occur quickly.<sup>8,9</sup>

### Screening and early detection

No, screening for brain tumours in healthy people with no symptoms is not feasible.

Screening is most effective for cancers that are common, can be detected early using a specific, safe, reliable and cost-effective test, and can be treated effectively if detected early.

Unlike cervical cancer, breast cancer or bowel cancer, malignant brain tumours are not suitable for screening programs. There is no known cost-effective test and early detection

### Diagnosis

Identifying a brain tumor usually involves a neurological examination, brain scans, and/or an analysis of the brain tissue.

A **neurological examination** is a series of tests to measure the function of the patient s nervous system and physical and mental alertness. If responses to the exam are not normal, the doctor may order a brain scan or refer the patient to a neurologist or neurosurgeon, who will then order a brain scan.

A **brain scan** is a picture of the internal structures in the brain. A specialized machine takes a scan in much the same way a digital camera takes a photograph. Using computer technology, a scan compiles an image of the brain by photographing it from various angles.

Some types of scans use a contrast agent (or contrast dye), which helps the doctor see the difference between normal and abnormal brain tissue. The contrast agent is injected into a vein and flows into brain tissue. Abnormal or diseased brain tissue absorbs more dye than normal healthy tissue. The most common scans used for diagnosis are as follows:

**MRI (Magnetic Resonance Imaging)** is a scanning device that uses magnetic fields and computers to capture images of the brain on film. It provides pictures from various planes, which permit doctors to create a three-dimensional image of the tumor.

**CT or CAT Scan (Computed Tomography)** combines sophisticated x-ray and computer technology. CT can show a combination of soft tissue, bone, and blood vessels. CT images can determine some types of tumors, as well as help detect swelling, bleeding, and bone and tissue calcification.

**PET Scan (Positron Emission Tomography)** provides a picture of the brain s activity, rather

than its structure, by measuring the rate at which a tumor absorbs glucose (a sugar). The patient is injected with deoxyglucose that has been labeled with radioactive markers. The PET scan measures the brain's activity and sends this information to a computer, which creates a live image.

A **biopsy** is a surgical procedure in which a sample of tissue is taken from the tumor site and examined under a microscope. The biopsy will provide information on types of abnormal cells present in the tumor. The purpose of a biopsy is to discover the type and grade of a tumor. A biopsy is the most accurate method of obtaining a diagnosis.

Once a sample is obtained, a pathologist examines the tissue under a microscope and writes a **pathology report** containing an analysis of the brain tissue. Sometimes the pathologist may not be able to make an exact diagnosis. This may be because more than one grade of tumor cells exists within the same tumor. In some cases, the tissue may be sent to another institution for additional analysis.<sup>10</sup>

### 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 that cannot be removed by surgery alone.

### Observation

Sometimes the best treatment is observation. For example, benign, slow growing tumors that are small and have few symptoms may be observed with routine MRI scans every year until their growth or symptoms necessitate surgery. Observation may be the best option for older patients with other health conditions.

### Medication

Medications are used to control some of the common side effects of brain tumors.

- Corticosteroid medications, such as dexamethasone (Decadron), are prescribed to reduce swelling and inflammation around the tumor. Because steroid medications can cause stomach

ulcers and gastric reflux, famotidine (Pepcid) or pantoprazole (Protonix) are prescribed to reduce the amount of acid produced in the stomach.

- Furosemide (Lasix) or mannitol (Osmitrol) may be used to control edema and intracranial pressure.
- Anticonvulsant medications are used to prevent or control seizures. The most common ones include phenytoin (Dilantin), valproic acid (Depakote), carbamazepine (Tegretol), and levetiracetam (Keppra).<sup>11</sup>

### 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 image-guided 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. Patients return daily over several weeks to receive the complete radiation dose.
- **Whole brain radiotherapy (WBRT)** delivers the radiation dose to the entire

brain. It is often used to treat multiple brain tumors and metastases.<sup>12</sup>

### 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. Chemotherapy is not routinely used for benign tumors.<sup>13</sup>

### Adjunct therapies

- Immunotherapy or biotherapy activates the immune system (T-cells and antibodies) to destroy cancer cells. Experimental research is exploring ways to prevent or treat cancer through vaccines.
- Gene therapy uses viruses or other vectors to introduce new genetic material into tumor cells. This experimental therapy can cause tumor cells to die or increase their susceptibility to other cancer therapies.
- Hyperbaric oxygen uses oxygen at higher than normal levels to promote wound healing and help fight infection. It may also improve the tumor's responsiveness to radiation and is being studied experimentally. Currently it is being used to help the body naturally remove dead tumor cells and treat radiation necrosis.<sup>14</sup>

### CONCLUSION

Malignant brain tumors include a variety of tumor types with specific chemotherapy regimens based on the pathologic diagnosis. All too often, health

care professionals and the public consider chemotherapy treatments for brain tumor patients to be futile. Recent advances with chemotherapy trials have already provided patients with new treatment options that can extend survival and improve quality of life, with a decrease in potential toxicities. Additionally, the current focus on the use of cytostatic agents and small-molecule therapies provide a renewed optimism that these novel therapies will improve outcomes for patients with malignant brain tumors. Early and accurate diagnosis of brain tumor is the key for implementing successful therapy and treatment planning. In the recent past several research works have been done for the diagnosis and treatment of brain tumor. It is expected that the information of new imaging technique MRI, C Tscan, PET scan helps in early detection and will give more accurate results.

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