CHAPTER 2

BRAIN TUMOR

2.1 INTRODUCTION

An abnormal growth of cells in the brain is called a brain tumor. A brain tumor consists of a collection of abnormally functioning brain cells that have begun to grow and reproduce inappropriately[1,5]. The uncontrolled growth of group of cells compresses and damages normal brain structures, which causes a variety of neurological symptoms.

According to the reports of National Cancer Institute, Primary brain tumors are the leading cause of tumor cancer deaths in children, now surpassing acute lymphoblast leukemia and are the third leading cause of cancer death in young adults ages 20 to 39.

2.2 CLASSIFICATION

There are more than 120 different types of brain tumors, making effective treatment very complicated. As per classification system defined by World Health Organization (WHO), brain tumor is named for the cell type of origin[2,3]. Brain
tumors can either originate from within the brain or from cancer cells that have metastasized from other organs or tissues.

Brain Tumors are broadly classified as below:

i) Benign brain tumors

ii) Malignant brain tumors

The terms benign and malignant are quite misleading when applied to brain tumor. Generally, for other organs, benign tumors are considered as harmless mass of tissues whereas malignant tumor is supposed to be cancerous. But, for brain tumor, both benign and malignant tumors have proved to be fatal and may lead to death[5].

The clinical features of these tumors are explained below.

i) Benign brain tumor consists of cells that have almost normal appearance when viewed under a microscope. The tumor is very slow-growing, has distinct borders that form a capsule and does not spread into adjacent brain tissue[9,11]. However, benign brain tumors can cause brain damage or be considered life-threatening due to their ability to encroach into areas of the brain occupied by normal cells, causing increased pressure on these cells. The most common benign brain tumors are meningiomas and neural sheath tumors, neurilemmoma.

ii) Malignant brain tumor grows and invades adjacent normal brain tissue but rarely spreads outside the brain. These tumors can be slow or fast growing and are usually life threatening due to their ability to infiltrate and destroy normal brain tissue. Malignant brain tumors can spread to other locations in the brain and spine because they lack distinct borders and are difficult to remove without prohibitive damage to normal brain tissue[12].

Malignant tumors can either originate from within brain cells or from cancer cells that have migrated from other organs or tissues. Depending on the origin of tumor, Malignant Brain tumors are further classified as Primary Brain Tumors and Secondary Brain Tumors.

Primary brain tumors originate from brain cells and can be derived from over twenty different cell types of brain. They are named and categorized by the type of cells that produce them. Primary brain tumors rarely metastasize outside the central nervous system, but it spreads within the brain[2,13]. Primary brain tumors do vary significantly
in terms of how rapidly they grow and spread. Thus, most primary brain tumors are described in terms of ‘grade.’ **Tumor Grade** is determined by the degree to which the tumor cells appear different from normal cells when viewed under the microscope. Grade is an important factor because the extent to which the cancer has differentiated or mutated compared to normal cells, may help determine the best possible treatment option.

Low-grade tumors tend to grow slowly and frequently remain dormant for long periods of time, while high-grade tumors grow and spread rapidly. High grade tumors generally invade neighboring normal brain tissue; therefore complete removal of tumor is not possible without removing an unacceptably large amount of normal brain tissue as well[5,9]. As brain is the central controlling organ of the body, damage of even a small normal brain tissue may result in some physical disorder or disability.

**Grade I tumors:** Grade I tumors are the least malignant, meaning they appear almost normal when viewed under a microscope. These tumors grow slowly and are usually associated with good long-term survival. **Pilocytic astrocytoma**, **Craniopharyngioma**, and many tumors of neurons, such as **Gangliocytoma** and **Ganglioglioma**, are examples of grade I tumors[11]. Figure 2.1 shows an image of grade I tumor, **Pilocytic astrocytoma**.

![Fig. 2.1 Pilocytic astrocytoma tumor (Grade I)](image)

**Grade II tumors:** These tumors have a slightly abnormal appearance when viewed under a microscope and are relatively fast growing as compared to grade tumors. Grade II tumors are well-differentiated and have distinct boundaries and are not as aggressive
as high-grade tumors[5]. However, they can invade adjacent normal tissue and sometimes these tumors recur as a higher grade as shown in Fig. 2.2

Fig. 2.2 Grade II tumor

**Grade III tumors (anaplastic):** These are, by definition, malignant, but there isn’t always a sharp distinction between a grade II and a grade III tumor[2]. The cells of a grade III tumor are actively reproducing abnormal cells and spreading into adjacent normal brain tissue. These tumors tend to recur, often as a higher grade. Fig. 2.3 displays grade III tumor.

Fig. 2.3 Grade III tumor

**Grade IV tumors (blastomas):** The most malignant tumors are designated as grade IV[6]. They have a bizarre appearance when viewed under the microscope, reproduce rapidly, and permeate adjacent normal brain tissues. These tumors induce the formation of new blood vessels so that they can maintain their rapid growth. They also have areas of dead cells in their center. Figure 2.4 shows the tumor image of Glioblastoma multiforme.
Grade IV tumors are commonly called as ‘Blastomas’. Fig. 2.4 shows the most common type of grade IV Glioblastoma Multiforme (GBM) is an aggressive and the most common type of brain tumor affecting mostly adults with a median age at diagnosis of 55 years. Gliomas account for 40% of primary and 78% of malignant brain tumors.

Secondary brain tumors metastasize from other organs or tissues. The most common forms of cancer that produce secondary brain tumors include lung, breast, kidney, and skin (melanoma) cancer. Central Nervous System metastasizes usually occur by way of the bloodstream. A cancer cell may break away from the original location in the body and travel in the circulatory system until it gets lodged in a small capillary network in brain tissue[6,8]. The cancers that most commonly metastasize to the brain are breast and lung cancer. During year 1976-1986, 50% of all CNS tumors were primary and 50% metastatic (secondary).

2.3 EPIDEMIOLOGY OF BRAIN TUMOR

Primary brain tumors represent about 1% of all cancers and 2.5% of all cancer deaths. Primary brain cancer is the second most common cause of cancer death between birth and the age of 34 and the fourth most common cause of cancer death in men aged 35-54. The overall incidence of all primary brain tumors is 141 per 100,000 people per year [3,4].

The exact causes of brain tumors are not known. However, it is clear that brain tumors are not contagious. Research has shown that people with certain risk factors are more likely than others to develop a brain tumor. The risk factors associated with an increased chance of developing a primary brain tumor are family history, exposure to
radiations or chemicals like Formaldehyde Vinyl chloride[5]. Acrylonitrile Brain tumors are more common in males than females. However, meningiomas are more common in females.

The symptoms of brain tumor depend upon the nature and site or position of tumor. Excessive growth of tumor generates intracranial pressure on surrounding brain tissue. This leads to the symptoms of focal epilepsy, monoplegia, cerebellar deficiency. The most common symptoms include headaches, nausea or vomiting, seizures or convulsions, difficulty in thinking, speaking, or finding words, personality changes, weakness or paralysis in one part or one side of the body, loss of balance, vision changes, confusion and disorientation, and memory loss[5,10]. Various tissues of the brain control different functions, so symptoms will vary depending on the tumor's location.

For early detection of Brain Tumor, at this time there are no blood tests or other screening exams that can be used routinely to detect brain tumors before they start to cause symptoms[6]. These tumors usually come to light as a result of signs or symptoms the person is having. In most cases, the patient's survival is determined by their age, the type of tumor, and its location. Earlier detection and treatment definitely improves chances of patient’s survival.

2.3.1 Survival rates for selected brain and spinal cord tumors

The statistics given below come from the Central Brain Tumor Registry of the United States (CBTRUS) and are based on people who were treated between 1973 and 2002 [3].

| Table 2.1 -Year Relative Survival Rate of brain tumor patients |
|-----------------|----------------|----------------|----------------|
| Age             |                |                |                |
| Type of Tumor   | 20-44   | 45-54   | 55-64   |
| Low-grade (diffuse) astrocytoma | 57%    | 37%     | 10%     |
| Anaplastic astrocytoma | 48%    | 26%     | 5%      |
| Glioblastoma multiforme | 13%    | 3%      | 1%      |
| Oligodendroglioma | 81%    | 66%     | 45%     |
| Anaplastic oligodendroglioma | 56%    | 46%     | 23%     |
2.4 ETIOLOGY AND PATHOLOGY OF BRAIN TUMOR

Brain tumors have a wide range of appearances and effect as enormous types of brain tumors exist. Brain tumors vary greatly in size and position. Their appearance varies in multispectral magnetic resonance images due to overlapping intensity variations. They may be space occupying or infiltrating. Infiltration of tumor into normal tissue may change properties of normal tissue. In some cases, tumor may be accompanied by surrounding edema (swelling). They may enhance fully, partially with contrast agent [11,12].

Etiology of some of the common primary and secondary tumors is reviewed here.

I. Secondary or Metastatic tumors: More than 50% of brain tumors are secondary or metastatic tumors, normally originating from lung, breast, kidney or intestine[6]. They are pinkish, rounded and well defined from the surrounding brain tissue.

II. Primary tumors: The most common type of primary tumors, Gliomas, are infiltrative tumors. Due to this the complete surgical removal of these tumors is difficult. Etiology of some of the common primary tumors as explained.

Astrocytoma is a white infiltrating growth that may occur at any age and in either the cerebral or cerebellar hemispheres. Astrocytomas grow slowly and are liable to undergo cystic transformation[2].

Glioblastoma Multiforme is an extremely malignant gliomas arising in middle age and is invariably found in the cerebral hemispheres. It is a reddish, highly vascular tumor that tends to infiltrate the brain extensively[13]. Microscopically, it consists of relatively undifferentiated round or oval cells.

Medulloblastoma is a rapidly growing tumor, frequently founding the cerebellum in children. It is composed of round undifferentiated cells.
Oligodendroglioma is a slow growing tumor that occurs in the cerebral hemisphere of young adults. It shows a tendency to calcification.

Ependymoma is a tumor arising from the ependyma in the roof of the fourth ventricle. It is firm whitish in colour.

Meningioma is an extracerebral tumor. It is composed of specialized connective tissue cells characteristically arranged in columns or whorls. The Meningioma is a single large irregularly lobulated growth as shown in Figure 2.6.
2.5 TYPES OF PRIMARY BRAIN TUMOR

The main types of primary brain tumors are Gliomas and Non-glial Brain Tumors

2.5.1 Gliomas

About half of all primary brain tumors and about one-fifth of all primary spinal cord tumors are gliomas, meaning that they grow from glial cells. Glial cells provide supportive functions for the neurons. Figure 2.7 shows glioma.

![Fig. 2.7 Glioma.](image)

Astrocytomas are the most common form of glioma and the most common type of primary brain tumor and is shown in Figure 2.8. These tumors can develop in any part of the central nervous system: the brain, brain stem, or spinal cord. Astrocytomas are further classified based on how the cells look under a microscope. Cells that are well differentiated mean that they have clear boundaries and structure.

![Fig. 2.8 Astrocytomas](image)
(i) **Non-invasive astrocytoma**: Non-invasive astrocytomas are tumors that grow slowly and usually do not grow into the tissues around them. There are two types of non-invasive astrocytomas called *juvenile pilocytic* and *subependymal*.

(ii) **Diffuse astrocytoma (stage I-II astrocytoma)**: Diffuse astrocytomas contain cells that are relatively normal and are considered to be low-grade tumors. They grow relatively slowly and may sometimes be completely removed through surgery. However, even well-differentiated astrocytomas can be life-threatening if they are inaccessible. In some cases, these tumors can also progress or recur as higher grade tumors[1].

(iii) **Anaplastic astrocytoma (stage III astrocytoma)**: grow more rapidly than low-grade tumors and contain cells with malignant traits, meaning they appear very different from normal cells when viewed under a microscope[6].

(iv) **Glioblastoma multiforme (stage IV astrocytoma, GBM)**: The most advanced stage of astrocytoma is called *Glioblastoma Multiforme*, or GBM. These tumors grow rapidly, invade nearby tissue and contain cells that are very malignant. GBM is among the most common and devastating primary brain tumors that affect adults. **Recurrent glioblastoma multiforme**: GBM that has returned or advanced after initial treatment is considered to be recurrent disease [6]. Recurrent GBM may occur after initial treatment of a lower grade astrocytoma, such as diffuse or anaplastic.

b. **Ependymomas**: Brain tumors that develop from cells that line the hollow cavities of the brain and the canal containing the spinal cord are called ependymomas as shown in Figure 2.9.. Most of these tumors are usually benign (non-cancerous) and slow growing.

(i) **Well-differentiated ependymoma (stage II)**: Well-differentiated ependymomas have cells that look very much like normal cells and grow slowly. (ii) **Anaplastic ependymoma (stage III)**: Anaplastic ependymomas are ependymal tumors that do not look like normal cells and grow more quickly than well-differentiated ependymal tumors.
c. Ependymoblastoma (stage IV): Ependymoblastomas are rare cancers that usually occur in children. They may grow very quickly.

d. Oligodendroglioma: Oligodendroglioma tumors begin in the brain cells called oligodendrocytes, which provide support and nourishment for the cells that transmit nerve impulses. It is shown in Figure 2.10.

2.5.2 Non-glial Brain Tumors

(i) Craniopharyngiomas: Another tumor that develops in the region of the pituitary gland near the hypothalamus is called a craniopharyngioma. These tumors are usually benign; however, they are sometimes considered malignant because they can press on or damage the hypothalamus and affect vital functions. These tumors occur most often in children and adolescents[3].
(ii) **Germ cell tumors:** Germ cell tumors arise from developing sex cells, called germ cells. There are different kinds of germ cells, including *germinomas, embryonal carcinomas, choriocarcinomas,* and *teratomas.*

(iii) **Meningiomas:** Meningiomas are very common brain tumors that occur in the membranes that cover and protect the brain and spinal cord (the meninges). Meningiomas usually grow slowly and tend to affect more women than men. Most meningiomas are considered to be benign tumors; however, even benign brain tumors can cause disability and may sometimes be life-threatening. Malignant meningioma is a rare tumor that grows more quickly than benign meningiomas[5]. Types of malignant meningioma include anaplastic meningioma, hemangiopericytoma and papillary meningioma.

(iv) **Pineal tumors:** Pineal region tumors are tumors found in or around the pineal, gland, a tiny organ located near the center of the brain that mediates changes in energy with light and darkness, causing sleepiness with darkness and alertness with increasing light as shown in Figure 2.11. The tumors can be slow-growing (*pineocytomas*) or fast-growing (*pineoblastomas*)[9]. The pineal region is very difficult to reach, and these tumors often cannot be removed.

![Fig. 2.11 Pineal tumors](image)

(v) **Pituitary adenomas:** The pituitary gland is a small, pea-sized structure located at the base of the brain in the center of the head, behind the eyes shown in figure. It is very important because it secretes several chemical messengers known as hormones, which help control the body's other glands and regulate growth, metabolism, maturation, and other essential body processes. Cancers of the pituitary gland are called pituitary adenomas[1]. Almost all adenomas are benign, but their slow expansion compresses
normal structures that surround it, suppressing normal pituitary function and sometimes causing headaches or problems with vision. Figure 2.12 shows pituitary tumor.

![Fig. 2.12 Pituitary tumors](image)

(vi) **Primitive neuroectodermal tumors (PNET):** PNETs are rare tumors that occur in children and young adults. The most common type of PNET is **medulloblastoma,** which arises from developing nerve cells that normally do not remain in the body after birth. These brain tumors begin in the lower part of the brain and may spread from the brain to the spine.

(vii) **Schwannomas:** Tumors that begin in Schwann cells, which produce the myelin that protects the acoustic nerve (nerve of hearing), are called schwannomas and are typically benign. **Acoustic neuromas** are a type of schwannoma. They occur mainly in adults and affect women twice as often as men.

**SUMMARY**

A brain tumor consists of a collection of abnormally functioning brain cells that have begun to grow and reproduce inappropriately. The uncontrolled growth of group of cells compresses and damages normal brain structures, which causes a variety of neurological symptoms. Brain Tumors are broadly classified as benign brain tumors and malignant brain tumors.

Benign brain tumor is very slow-growing, has distinct borders that form a capsule and does not spread into adjacent brain tissue. However, benign brain tumors can cause brain damage or be considered life-threatening due to their ability to encroach into areas of the brain occupied by normal cells, causing increased pressure on these cells. The most common benign brain tumors are meningiomas and neural sheath tumors, neurilemmoma.
Malignant brain tumor grows and invades adjacent normal brain tissue but rarely spreads outside the brain. These tumors can be slow or fast growing and are usually life threatening due to their ability to infiltrate and destroy normal brain tissue. Malignant Brain tumors are further classified as Primary Brain Tumors and Secondary Brain Tumors. Primary brain tumors originate from brain cells and can be derived from over twenty different cell types of brain. Most primary brain tumors are described in terms of grade. Grade I,II,III and IV are commonly detected brain tumors. Tumor Grade is determined by the degree to which the tumor cells appear different from normal cells when viewed under the microscope.