



REVIEW ARTICLE

PHARMACOLOGY

REVIEW OF BRAIN AND BRAIN CANCER TREATMENT*Corresponding Author****R.Srinivasan*****Siddhartha institute of pharmaceutical sciences, Jonnalagadda,
Narasaraopet, Guntur***Co Authors****L. Manoj, M.Kalyani, K.Jyothi, G.Ganga Bhavani and V.Govardhani*****Siddhartha institute of pharmaceutical sciences, Jonnalagadda, Narasaraopet, Guntur****ABSTRACT**

The brain and spinal column make up the central nervous system (CNS), where all vital functions of the body are controlled. When tumors arise in the central nervous system, they are especially problematic because a person's thought processes and movements can be affected. These tumors can also be difficult to treat because the tissues surrounding a tumor that may be affected by surgery or radiation may play a vital role in functioning. There are two broad types of cancers occurring within this system. Primary tumors originate in the central nervous system, whereas secondary tumors migrate from cancers located elsewhere in the body, such as breast cancers. Secondary, or metastatic, brain tumors, are more common than primary brain cancers. This section focuses on primary stages on brain cancer.



KEYWORDS

Brain, Cancer, Tumour

INTRODUCTION

The brain and spinal cord form the central nervous system this complex system is part of everything we do. It controls the things we choose to do, like walk and talk, and the things our body does automatically, like breathe and digest food. The central nervous system is also involved with our senses; seeing, hearing, touching, tasting, and smelling, as well as our emotions, thoughts, and memory.

The brain is a soft, spongy mass of nerve cells and supportive tissue. It has three major parts: the cerebrum, the cerebellum, and the brain stem. The parts work together, but each has special functions.

The brain is composed of:

- A. The cerebrum, which is divided into two cerebral hemispheres. The cerebrum is the largest part of the brain and is divided into lobes where discrete functions occur. Higher reasoning takes place in the cerebrum.
- B. The cerebellum, or little brain, located beneath the cerebrum. The cerebellum controls coordination and balance.
- C. The brain stem, which is the lowest portion of the brain and connects to the spinal cord, controls involuntary functions essential for life, such as the beating of the heart and breathing.
- D. The meninges, membranes that surround and protect the brain and spinal cord. There are three meninges.

The types of **primary brain cancers** are classified according to the type of cells from which they originate. Oncologists describe the tumor based on its characteristics. For example, a noninfiltrating tumor can be expected to grow slowly and not invade surrounding structures. A well-differentiated tumor is also slow growing,

but has the potential to be invasive. Anaplastic tumors are generally more aggressive.

Gliomas - Most brain tumors are gliomas, which originate in the glial cells (the supportive cells of the nervous system). Gliomas can be described as low-grade (slow-growing); intermediate-grade (more aggressive); or high-grade (very aggressive).

There are many different types of gliomas:

- E. **Astrocytoma**, the most common type of glioma, which usually begin in cells called astrocytes within the cerebrum, or the cerebellum. Glioblastoma multiforme is a form of very aggressive astrocytoma.
- F. **Oligodendroglioma**, a tumor that develops from oligodendrocytes. These cells are responsible for producing the myelin that surrounds nerves.
- G. **Brain stem glioma**, which begins in the glial cells in the brain stem.
- H. **Ependymoma**, which begins in the ependyma, the cells that line the passageways in the brain where cerebrospinal fluid is made and stored.
- I. **Mixed tumors**, which are composed of more than one of the glial cell types.

Nonglial tumors include:

- J. **Acoustic schwannoma**, which occurs in the vestibular nerve.
- K. **Craniopharyngioma**, which begins near the pituitary gland.
- L. **Meningiomas**, which originate in the meninges surrounding the brain and spinal column. Even though these tumors are generally benign, they may cause significant symptoms as they grow and press on the brain or spinal cord.



M. **Medulloblastoma**, which arises from granular cells in the cerebellum.

N. **Primary CNS lymphoma**.

O. The pineal and pituitary glands, located near the base of the brain, can also be the sources of tumours

COMPARISION BETWEEN NORMAL CELLS AND CANCER CELLS

Normal Cells	Cancer Cells
DNA in genes and chromosomes go about their business in a normal way.	Cancer cells develop a different DNA or gene structure or acquire abnormal numbers of chromosomes.
Cells divide in an orderly way to produce more cells only when the body needs them.	Cells continue to be created without control or order. If not needed, a mass of tissue is formed which is called a tumor.
Energy	
Normal Cells	Cancer Cells
Cells derive 70% of their energy from a system called the "Krebs Cycle."	Cells have a defective "Krebs Cycle" and derive little or no energy from it.
Cells derive only 20% of their energy from a system called "Glycolosis."	Cancer cells derive almost all their energy from "Glycolosis."
Cells derive most of their energy with the use of oxygen.	Cells derive most of their energy in the absence of oxygen.
Blood Vessels	
Normal Cells	Cancer Cells
Cells have a built-in blood vessel system.	Cells do not have a built-in blood vessel system. They require more of certain amino acids to grow.
Growth Factors	
Normal Cells	Cancer Cells
While similar to cancer cells, the amount of them is more in balance to produce a more normal level of activity.	These cells have over produced, require more chemicals (food) and are over active.
Functions	
Normal Cells	Cancer Cells
The enzymes and hormones go about business in a normal balanced manner.	The enzymes and hormones are either over active or under active.
Tumors are Different	
Benign	Malignant
Benign tumors are not cancerous. They do not invade nearby tissues nor spread to other parts of the body. They can be removed and are not a threat to life.	Malignant tumors are cancerous. They can invade and damage nearby tissues and organs and they can break away and enter the blood stream to form new tumors in other parts of the body. The spread of cancer is called metastasis.



CAUSES OF BRAIN TUMOURS

The causes of brain tumors are not known. Researchers are trying to solve this problem. The more they can find out about the causes of brain tumors, the better the chances of finding ways to prevent them.

Doctors cannot explain why one person gets a brain tumor and another doesn't, but they do know that no one can "catch" a brain tumor from another person. Brain tumors are not contagious.

Although brain tumors can occur at any age, studies show that they are most common in two age groups. The first group is children 3 to 12 years old; the second is adults 40 to 70 years old.

By studying large numbers of patients, researchers have found certain risk factors that increase a person's chance of developing a brain tumor. People with these risk factors have a higher-than-average risk of getting a brain tumor. For example, studies show that some types of brain tumors are more frequent among workers in certain industries, such as oil refining, rubber manufacturing, and drug manufacturing. Other studies have shown that chemists and embalmers have a higher incidence of brain tumors. Researchers also are looking at exposure to viruses as a possible cause. Because brain tumors sometimes occur in several members of the same family, researchers are studying families with a history of brain tumors to see whether heredity is a cause. At this time, scientists do not believe that head injuries cause brain tumors to develop.

In most cases, patients with a brain tumor have no clear risk factors. The disease is probably the result of several factors acting together.

PRIMARY BRAIN TUMOURS

Tumors that begin in the brain tissue are known as primary brain tumors. Secondary tumors are those that develop when cancer spreads to the brain. Primary brain tumors are classified by the type of tissue in which they

begin. The most common brain tumors are gliomas, which begin in the glial (supportive) tissue. There are several types of gliomas:

Astrocytomas arise from small, star-shaped cells called astrocytes. They may grow anywhere in the brain or spinal cord. In adults, astrocytomas most often arise in the cerebrum. In children, they occur in the brain stem, the cerebrum, and the cerebellum. A grade III astrocytoma is sometimes called anaplastic astrocytoma. A grade IV astrocytoma is usually called glioblastoma multiforme.

Brain stem gliomas occur in the lowest, stemlike part of the brain. The brain stem controls many vital functions. Tumors in this area generally cannot be removed. Most brain stem gliomas are high-grade astrocytomas. Ependymomas usually develop in the lining of the ventricles. They also may occur in the spinal cord. Although these tumors can develop at any age, they are most common in childhood and adolescence.

Oligodendrogliomas arise in the cells that produce myelin, the fatty covering that protects nerves. These tumors usually arise in the cerebrum. They grow slowly and usually do not spread into surrounding brain tissue. Oligodendrogliomas are rare. They occur most often in middle-aged adults but have been found in people of all ages.

There are other types of brain tumors that do not begin in glial tissue. Some of the most common are described below:

- Medulloblastomas were once thought to develop from glial cells. However, recent research suggests that these tumors develop from primitive (developing) nerve cells that normally do not remain in the body after birth.
- Meningiomas grow from the meninges. They are usually benign. They occur most often in women between 30 and 50 years of age.
- Schwannomas are benign tumors that begin in Schwann cells. Acoustic neuromas



are a type of schwannoma. They occur mainly in adults. These tumors affect women twice as often as men.

- Craniopharyngiomas develop in the region of the pituitary gland near the hypothalamus. These tumors occur most often in children and adolescents.
- Germ cell tumors arise from primitive (developing) sex cells, or germ cells. The most frequent type of germ cell tumor in the brain is the germinoma.

SECONDARY BRAIN TUMOURS

Metastasis is the spread of cancer. Cancer that begins in other parts of the body may spread to the brain and cause secondary tumors. These tumors are not the same as primary brain tumors. Cancer that spreads to the brain is the same disease and has the same name as the original (primary) cancer. For example, if lung cancer spreads to the brain, the disease is called metastatic lung cancer because the cells in the secondary tumor resemble abnormal lung cells, not abnormal brain cells.

Treatment for secondary brain tumors depends on where the cancer started and the extent of the spread, as well as other factors, including the patient's age, general health, and response to previous treatment.

ADULT BRAIN TUMOURS

Adult brain tumors are diseases in which cancer (malignant) cells begin to grow in the tissues of the brain. The brain controls memory and learning, senses (hearing, sight, smell, taste, and touch), and emotion. It also controls other parts of the body, including muscles, organs, and blood vessels. Tumors that start in the brain are called primary brain tumors.

METASTATIC BRAIN TUMOURS

Often, tumors found in the brain have started somewhere else in the body and spread (metastasized) to the brain. These are called metastatic brain tumors.

SYMPTOMS OF ADULT BRAIN TUMOURS

- Frequent headaches.
- Vomiting.
- Loss of appetite.
- Changes in mood and personality.
- Changes in ability to think and learn.
- Seizures.

Treatment of brain tumor depends on a number of factors. Among these are the type, location, and size of the tumor, as well as the patient's age and general health. Treatment methods and schedules often vary for children and adults. A treatment plan is developed to fit each patient's needs.

TESTS TO DETECT BRAIN TUMOURS

Tests that examine the brain and spinal cord are used to detect (find) adult brain tumor. The following tests and procedures may be used:

- CT scan (CAT scan): A procedure that makes a series of detailed pictures of areas inside the body, taken from different angles. The pictures are made by a computer linked to an x-ray machine. A dye may be injected into a vein or swallowed to help the organs or tissues show up more clearly. This procedure is also called computed tomography, computerized tomography, or computerized axial tomography.
- MRI (magnetic resonance imaging): A procedure that uses a magnet, radio waves, and a computer to make a series of detailed pictures of the brain and spinal cord. A substance called gadolinium is injected into the patient through a vein. The gadolinium collects around the cancer cells so they show up brighter in the picture. This procedure is also called nuclear magnetic resonance imaging (NMRI).

Adult brain tumor is diagnosed and removed in surgery. If a brain tumor is suspected, a biopsy is done by removing part of the skull and using a needle to remove a sample of the brain tissue. A pathologist views the tissue under a



microscope to look for cancer cells. If cancer cells are found, the doctor will remove as much tumor as safely possible during the same surgery. An MRI may then be done to determine if any cancer cells remain after surgery. Tests are also done to find out the grade of the tumor.

GRADES OF A TUMOUR

The grade of a tumor refers to how abnormal the cancer cells look under a microscope and how quickly the tumor is likely to grow and spread. The pathologist determines the grade of the tumor using tissue removed for biopsy. The following grading system may be used for adult brain tumors:

Grade I : 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.

Grade II : The tumor grows slowly, but may spread into nearby tissue and may become a higher-grade tumor.

Grade III : The tumor grows quickly, is likely to spread into nearby tissue, and the tumor cells look very different from normal cells.

Grade IV : The tumor grows very aggressively, has cells that look very different from normal cells, and is difficult to treat successfully.

The chance of recovery (prognosis) and choice of treatment depend on the type, grade, and location of the tumor and whether cancer cells remain after surgery and/or have spread to other parts of the brain.

TREATMENT FOR ADULT BRAIN TUMOUR

Different types of treatment are available for patients with adult brain tumor. Some treatments are standard (the currently used treatment), and some are being tested in clinical trials. Before starting treatment, patients may

want to think about taking part in a clinical trial. A treatment clinical trial is a research study meant to help improve current treatments or obtain information on new treatments for patients with cancer. When clinical trials show that a new treatment is better than the standard treatment, the new treatment may become the standard treatment.

Three types of standard treatment are used.

1. Surgery

Surgery is used, when possible, to treat adult brain tumor

2. Radiation therapy

Radiation therapy is a cancer treatment that uses high-energy x-rays or other types of radiation to kill cancer cells. There are two types of radiation therapy. External radiation therapy uses a machine outside the body to send radiation toward the cancer. Internal radiation therapy uses a radioactive substance sealed in needles, seeds, wires, or catheters that are placed directly into or near the cancer. The way the radiation therapy is given depends on the type and stage of the cancer being treated.

3. Chemotherapy

Chemotherapy is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping the cells from dividing. When chemotherapy is taken by mouth or injected into a vein or muscle, the drugs enter the bloodstream and can reach cancer cells throughout the body (systemic chemotherapy). When chemotherapy is placed directly into the spinal column, an organ, or a body cavity such as the abdomen, the drugs mainly affect cancer cells in those areas (regional chemotherapy). A dissolving wafer may be used to deliver an anticancer drug directly into the brain tumor site after the tumor has been removed by surgery. The way the



chemotherapy is given depends on the type and stage of the cancer being treated.

TREATMENT FOR METASTATIC BRAIN TUMOURS

Tumors that have spread to the brain from somewhere else in the body are usually treated with radiation therapy and/or surgery. Chemotherapy may be used if the primary tumor is the kind that responds well to chemotherapy. Clinical trials are under way to study new treatments.

Brain Stem Gliomas

Treatment of brain stem gliomas may include the following:

1. Hyperfractionated radiation therapy.
2. A clinical trial of new anticancer drugs and/or biologic therapy.

Pineal Astrocytic Tumors

Treatment of pineal astrocytic tumors may include the following:]

1. Surgery and radiation therapy, with or without chemotherapy.
2. A clinical trial of external radiation therapy plus hyperthermia therapy or new methods of delivering radiation therapy.
3. A clinical trial of new anticancer drugs and biologic therapy following radiation therapy.

Pilocytic Astrocytomas

Treatment of pilocytic astrocytoma is usually surgery with or without radiation therapy.

Diffuse Astrocytomas

Treatment of diffuse astrocytoma may include the following:

1. Surgery, usually with radiation therapy.
2. A clinical trial of surgery and radiation therapy with or without chemotherapy for tumors that cannot be completely removed by surgery.
3. A clinical trial of radiation therapy delayed until the tumor progresses.
4. A clinical trial comparing high-dose and low-dose radiation therapy.

Anaplastic Astrocytomas

Treatment of anaplastic astrocytoma may include the following:

1. Surgery plus radiation therapy, with or without chemotherapy.
2. A clinical trial of external radiation therapy plus hyperthermia therapy or new methods of delivering radiation therapy.
3. A clinical trial of new anticancer drugs and biologic therapy following radiation therapy.
4. A clinical trial of chemotherapy combined with different methods of delivering radiation therapy.

Glioblastoma

Treatment of glioblastoma may include the following:

1. Surgery plus radiation therapy, with or without chemotherapy.
2. A clinical trial of chemotherapy placed into the brain during surgery.
3. A clinical trial of radiation and concurrent chemotherapy.
4. A clinical trial of external radiation therapy plus hyperthermia therapy or new methods of delivering radiation therapy.
5. A clinical trial of new anticancer drugs and biologic therapy following radiation therapy.
6. A clinical trial of chemotherapy and new methods of delivering radiation therapy.
7. Clinical trials of new treatments.

Oligodendroglial Tumors

Treatment of oligodendrogliomas may include the following:

1. Surgery, usually with radiation therapy.
2. A clinical trial of surgery and radiation therapy with or without chemotherapy for tumors that cannot be completely removed by surgery.

Treatment of anaplastic oligodendroglioma may include the following:

1. Surgery plus radiation therapy with or without chemotherapy.



2. A clinical trial of external radiation therapy plus hyperthermia therapy or new methods of delivering radiation therapy.
3. A clinical trial of new anticancer drugs and biologic therapy following radiation therapy.

Mixed Gliomas

Treatment of mixed gliomas may include the following:

1. Surgery plus radiation therapy with or without chemotherapy.
2. A clinical trial of external radiation therapy plus hyperthermia therapy or new methods of delivering radiation therapy.
3. A clinical trial of new anticancer drugs or biologic therapy following radiation therapy.

Ependymal Tumors

Treatment of grade I and grade II ependymomas is usually surgery with or without radiation therapy.

Treatment of anaplastic ependymoma may include the following:

1. Surgery plus radiation therapy.
2. A clinical trial of surgery followed by chemotherapy before, during, and after radiation therapy.
3. A clinical trial of chemotherapy and/or biologic therapy.

Medulloblastoma

Treatment of medulloblastomas may include the following:

1. Surgery plus radiation therapy to the brain and spine.
2. A clinical trial of surgery and radiation therapy to the brain and spine for tumors that are more difficult to treat successfully.
3. A clinical trial of chemotherapy.

Pineal Parenchymal Tumors

Treatment of pineal parenchymal tumors may include the following:

1. Surgery plus radiation therapy with or without chemotherapy.

2. A clinical trial of external radiation therapy plus hyperthermia therapy or new methods of delivering radiation therapy.
3. A clinical trial of new anticancer drugs and biologic therapy following radiation therapy.

Meningeal Tumors

Treatment of meningiomas may include the following:

1. Surgery with or without radiation therapy.
2. Radiation therapy for tumors that cannot be removed by surgery.

Treatment of malignant meningioma may include the following:

1. Surgery plus radiation therapy.
2. A clinical trial of external radiation therapy plus hyperthermia therapy or new methods of delivering radiation therapy.
3. A clinical trial of new anticancer drugs and/or biologic therapy following radiation therapy.

Germ Cell Tumors

Treatment of central nervous system germ cell tumors depends on the type of cancer cells, the location of the tumor, whether the cancer can be removed in an operation, and other factors.

Craniopharyngioma

Treatment of craniopharyngiomas may include the following:

1. Surgery to remove the entire tumor.
2. Surgery to remove as much of the tumor as possible, followed by radiation therapy.

Recurrent Adult Brain Tumor

Treatment of recurrent adult brain tumors may include the following:

1. Surgery with or without chemotherapy.
2. Radiation therapy, if not used during previous treatment, with or without chemotherapy.
3. Internal radiation therapy.
4. Chemotherapy.



5. A clinical trial of new anticancer drugs.
6. A clinical trial of chemotherapy placed into the brain during surgery.
7. A clinical trial of biologic therapy.

Metastatic Brain Tumors

Treatment of a single metastatic brain tumor is usually surgery followed by radiation therapy to the brain.

Treatment of more than one metastatic brain tumor may include the following:

1. Radiation therapy to the brain.
2. Surgery, for large tumors that are pressing on areas of the brain and causing symptoms.

SIDE EFFECTS IN CANCER TREATMENT

Cancer treatment often causes side effects. These side effects occur because treatment to destroy cancer cells damages some healthy cells as well. The side effects of cancer treatment vary. They depend on the type of treatment used and on the area being treated. Also, each person reacts differently. Attempts are made to plan the patient's therapy to keep side effects to a minimum. Patients are very carefully watched so that any problems which occur can be addressed.

A craniotomy is a major operation. The surgery may damage normal brain tissue, and edema may occur. Weakness, coordination problems, personality changes, and difficulty in speaking and thinking can result. Patients can also have seizures. In fact, for a short time after surgery, symptoms may be worse than before. Most of the side effects of surgery lessen or disappear with time.

Most of the side effects of radiation therapy go away soon after treatment is over. However, some side effects may occur or persist long after treatment is completed.

Some patients have nausea for several hours after treatment. Patients receiving radiation therapy may become very tired as treatment continues. Resting is important, but doctors usually advise their patients to try to stay reasonably active. Radiation therapy to the scalp

causes most patients to lose their hair. When it grows back, the new hair is sometimes softer and may be a slightly different color. In some cases, hair loss is permanent.

Skin reactions in the treated area are common. The scalp and ears may be red, itchy, or dark. These areas may look and feel sunburned. The treated area should be exposed to the air as much as possible but should be protected from the sun. Patients should not wear anything on the head that might cause irritation. Good skin care is important at this time. The doctor may suggest certain kinds of soap or ointment, and patients should not use any other lotions or creams on the scalp without the doctor's advice.

Sometimes, brain cells killed by radiation form a mass in the brain. The mass may look like a tumor and may cause similar symptoms, such as headaches, memory loss, or seizures. Doctors may suggest surgery or steroids to relieve these problems. About 4 to 8 weeks after radiation therapy, patients may become quite sleepy or lose their appetite. These symptoms may last several weeks, but they usually go away on their own. Still, patients should notify the doctor if they occur.

Children who have had radiation therapy for a brain tumor may have learning problems or partial loss of eyesight. If the pituitary gland is damaged, children may not grow or develop normally.

The side effects of chemotherapy depend on the drugs that are given. In general, anticancer drugs affect rapidly growing cells, such as blood cells that fight infection, cells that line the digestive tract, and cells in the hair follicles. As a result, patients may have a lowered resistance to infection, loss of appetite, nausea, vomiting, or mouth sores. Patients also may have less energy and lose their hair. These side effects usually go away gradually after treatment stops.

Some anticancer drugs can cause infertility. Women taking certain anticancer drugs may have symptoms of menopause (hot



flashes and vaginal dryness; periods may be irregular or stop). Some drugs used to treat children and teenagers may affect their ability to have children later in life.

Certain drugs used in the treatment of brain tumors can cause kidney damage. Patients are given large amounts of fluid while taking these drugs. Patients also may have tingling in the fingers, ringing in the ears, or difficulty hearing. These problems may not clear up after treatment stops.

Treatment with steroids to reduce swelling in the brain can cause increased appetite and weight gain. Swelling of the face and feet is common. Steroids can also cause restlessness, mood swings, burning indigestion, and acne. Patients should not stop using steroids or change their dose without consulting the doctor, however. The use of steroids must be stopped gradually to allow the body time to adjust.

Loss of appetite can be a problem for patients during therapy. People may not feel hungry when they are uncomfortable or tired. Some of the common side effects of cancer treatment, such as nausea and vomiting, can also make it hard to eat. Yet, good nutrition is important because patients who eat well

generally feel better and have more energy. In addition, they may be better able to withstand the side effects of treatment. Eating well means getting enough calories and protein to help prevent weight loss, regain strength, and rebuild normal tissues. Many patients find that eating several small meals and snacks during the day works better than trying to have three large meals.

Patients being treated for a brain tumor may develop a blood clot and inflammation in a vein, most often in the leg. This is called thrombo-phlebitis. A patient who notices swelling in the leg, leg pain, or redness in the leg should notify the doctor right away.

CONCLUSION

Brain is a delicate organ and it is the complex structure consisting of numerous parts. Each of its part has a specific function. Impairment of any part causes serious complications. More than fifteen thousand people are affected due to brain disorders. Hence any of the above treatment procedures is helpful in detecting and curing the diseases.

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