ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 11| November 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

THE CASE STUDY OF BRAIN TUMOR

Mr. Shubham G. Doifode[1], Mr. Sharad P. Kanhere[2], Dr. Sunil S. Jaybhaye[3], Dr. Swati Rawat[4], Mr. Abhishek R.Vanjare[5]

[1]*Guide*
[2]*Student*
[3]*Vice Principle of Institute Pharmacy Badnapur,Jalna*
[4]*Principle of Institute of Pharmacy Badnapur,Jalna*
[5]*Student*
Institute of Pharmacy, Badnapur , Jalna 431202

ABSTRACT

This project focuses on the development and evaluation of pharmaceutical strategies for the treatment of brain tumors. It encompasses the formulation of novel drug delivery systems, such as nanoparticles and liposomes, to enhance the targeted delivery of chemotherapeutic agents to the brain. The study aims to overcome challenges like the blood-brain barrier, drug resistance, and systemic toxicity. Key findings include improved drug bioavailability, enhanced tumor specificity, and reduced side effects, demonstrating the potential of advanced drug delivery platforms in brain tumor therapy. The project concludes with recommendations for clinical translation and further research in personalized medicine

KEYWORD:- *Brain tumor, type, india ,Canada ,treatment, prevention*

• INTRODUCTION

A brain tumor is a growth of cells in the brain or near it. Brain tumors can happen in the brain tissue. Brain tumors also can happen near the brain tissue. Nearby locations include nerves, the pituitary gland, the pineal gland, and the membranes that cover the surface of the brain.

Brain tumors can begin in the brain. These are called primary brain tumors. Sometimes, cancer spreads to the brain from other parts of the body. These tumors are secondary brain tumors, also called metastatic brain tumors.

Many different types of primary brain tumors exist. Some brain tumors aren't cancerous. These are called noncancerous brain tumors or benign brain tumors. Noncancerous brain tumors may grow over time and press on the brain tissue. Other brain tumors are brain cancers, also called malignant brain tumors. Brain cancers may grow quickly. The cancer cells can invade and destroy the brain tissue.

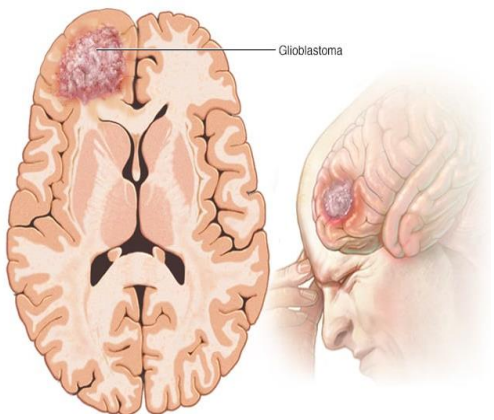
Brain tumors range in size from very small to very large. Some brain tumors are found when they are very small because they cause symptoms that you notice right away. Other brain tumors grow very large before they're found. Some parts of the brain are less active than others. If a brain tumor starts in a part of the brain that's less active, it might not cause symptoms right away. The brain tumor size could become quite large before the tumor is detected.
Brain tumor treatment options depend on the type of brain tumor you have, as well as its size and location. Common treatments include surgery and radiation therapy.

• Types Brain Tumor

There are many types of brain tumors. The type of brain tumor is based on the kind of cells that make up the tumor. Special lab tests on the tumor cells can give information about the cells. Your health care team uses this information to figure out the type of brain tumor

Some types of brain tumors usually aren't cancerous. These are called noncancerous brain tumors or benign brain tumors. Some types of brain tumors usually are cancerous. These types are called brain cancers or malignant brain tumors. Some brain tumor types can be benign or malignant.

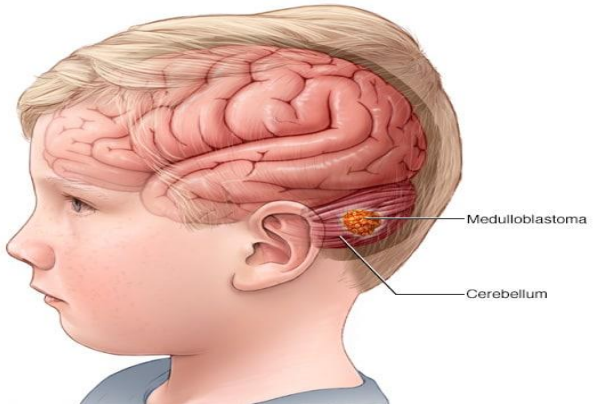
Benign brain tumors tend to be slow-growing brain tumors. Malignant brain tumors tend to be fast-growing brain tumors.



ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 11| November 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402|| ISI Value: 1.188

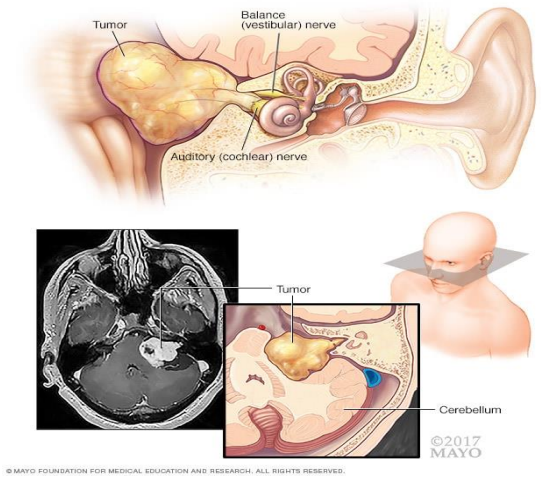
1.Glioblastoma

Glioblastoma is a type of cancer that starts in cells called astrocytes that support nerve cells. It can form in the brain or spinal cord.



2.Medulloblastoma

Medulloblastoma is a type of brain cancer that starts in the part of the brain called the cerebellum. Medulloblastoma is the most common type of cancerous brain tumor in children.



3.Acoustic Neuroma (Vestibular Schwannoma)

An acoustic neuroma (vestibular schwannoma) is a benign tumor that develops on the balance and hearing nerves leading from the inner ear to the brain. These nerves are twined together to form the vestibulocochlear nerve (eighth cranial nerve). The pressure on the nerve from the tumor may cause hearing loss and imbalance.

- **Types Brain tumor Gliomas and related brain tumors :** Gliomas are growths of cells that look like glial cells. The glial cells surround and support nerve cells in the brain tissue. Types of gliomas and related brain tumors include astrocytoma, glioblastoma, oligodendroglioma an d ependymoma. Gliomas can be benign, but most are malignant. Glioblastoma is the most common type of malignant brain tumor.
- **Choroid plexus tumors:** Choroid plexus tumors start in cells that make the fluid that surrounds the brain and spinal cord. This fluid is called cerebrospinal fluid. Choroid plexus tumors are located in the fluid-filled cavities in the brain, called the ventricles. Choroid plexus tumors can be benign or malignant. Choroid plexus carcinoma is the malignant form of this type of brain tumor. It's more common in children.
- **Embryonal tumors:** Embryona l tumors begin in cells that are left over from fetal development. The cells, called embryonal cells, stay in the brain after birth. Embryonal tumors are malignant brain tumors that happen most often in babies and young children. The most common type of

- **Introduction to Cancer in India**

Cancer is a major cause of morbidity and mortality in developing and developed countries alike.1 In many low-income and middle-income countries, including India, most of the population does not have access to a well organised and well regulated cancer care system. A diagnosis of cancer often leads to catastrophic personal health expenditures.2 Such expenditures can push entire families below the poverty line and may, especially when combined with an absence of what are seen as acceptable services, threaten social stability.

Population ageing is often assumed to be the main factor driving increases in cancer incidence, death rates, and health-care costs. 5 However, the actual picture is more complex. In high-income countries age-standardised cancer mortality is now typically decreasing in all age groups, although more than half of all cancer deaths are people older than 70 years. In India, despite the weakness of data in terms of population coverage, no evidence exists for a decrease in age-standardised cancer mortality rates, and most deaths occur in individuals younger than 70 years.1 These dierences are only partly due to India having a relatively younger population compared with high-income countries. They are also a product of con trasting causal patterns, with infections and unique local patterns of tobacco use playing a much greater part in causing cancer in India than in richer countries. Poor access to screening and early-stage case-finding services also helps to explain the paradox of India's seemingly low cancer incidence rates but relatively high age-specific death rates

Although improvements in living standards and Human Development Index rankings are typically linked to increases in the occurrence of, for example, sex hormone exposure-related cancers, and cancers epidemiologically associated with reduced average family sizes,6 the positive gains that economic and social development bring—eg, improved food quality—normally far outweigh any such costs. The International Agency for Research on Cancer GLOBOCAN project1 has predicted that India's cancer burden will nearly double in the next 20 years, from slightly over a million new cases in 2012 to more than 1·7 million by 2035. These projections indicate that the absolute number of cancer deaths will also rise from about 680 000 to 1·2 million in the same period.1 Yet the extent to which cancer-related mortality and disability will actually increase partly depends on the investment decisions made in future decades in health care, cancer research, the wider public understanding of cancer harm-reduction, and on other technical

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 11| November 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

or social changes that will arect disease incidence and outcomes. Here, we review publish.[2]

- **Introduction to Cancer in Canada**

Primary malignant brain tumours are among the most disabling and lethal types of cancer. Although they constitute only about 2% of all cancers brain tumours are associated with severe disability and a high risk of death. For all ages combined the median survival time is about 9 months and the 5-year survival rate less than 25%.' Many of the patients who are alive after 5 years are left with permanent disabilities.2 Moreover, survival rates have increased only slightly in recent years.

ates have increased only slightly in recent years.1'2 Brain cancer is of particular concern because of major increases in death and incidence rates ob served over the last few decades in Canada and in most developed countries.3-10 These increases are most pronounced among elderly people. Greig and associates"I reported major increases in the incidence of brain tumours in the US elderly population between 1973 and 1985. Davis and collaborators6 found an approximate threefold increase in the rate of death from brain cancer between 1968 and 1983 among US white people aged 75 to 84 years and a significant increase among those 65 to 74. Others reported similar trends in Norway'2 and England and Wales.'3 Two international studies of trends in the rate of death from brain cancer showed that increases were observed in most of the countries studied.

- **Material and Methods Mortality,**

incidence and hospital morbidity data were obtained from the Vital Statistics Section, the National Cancer Incidence Reporting System (NCIRS) and the Institutional Health Section of the Canadian Centre for Health Information. Annual population estimates were obtained from the Demo graphic Division of Statistics Canada. The study period was from 1959 to 1988 for mortality data, from 1969 to 1985 for incidence data and from 1971 to 1985 for hospital morbidity data.

The annual rates of brain cancer (International Classification of Diseases [ICD] code 19116) were calculated by sex and 5-year age groups for Canada and for each province. Broader age intervals were also examined. The direct method was-used to calculate age-adjusted rates, the 1971 Canadian pop ulation being the standard. A cohort analysis was performed for all cancers of the nervous system, since brain cancer was not available as a separate category within the ICD classification before 1959.

We analysed the geographic distribution of brain cancer by comparing death rates in census divisions with the national rates. The statistical significance of the age-standardized death rates was assessed with the use ofthe Fisher-Neyman test.'8 Survival rates were estimated on the basis of cases diagnosed in Saskatchewan between 1967 and 1986. The crude survival rates were calculated with the use of a life-table method and adjusted for the deaths expected to occur in the general Saskatche wan population according to the normal life expec tancy for that province.' Long-term (5-year, 10-year and 15-year) survival rates have been estimated and are published elsewhere.' However, because the me dian survival time of brain cancer patients is very low the 1-year, 2-year, 3-year and 4-year survival rates are more relevant clinically and are presented by age, calendar period and tumour type. The statistical significance of differences in relative survival rates was calculated on the basis of their relative standard errors.

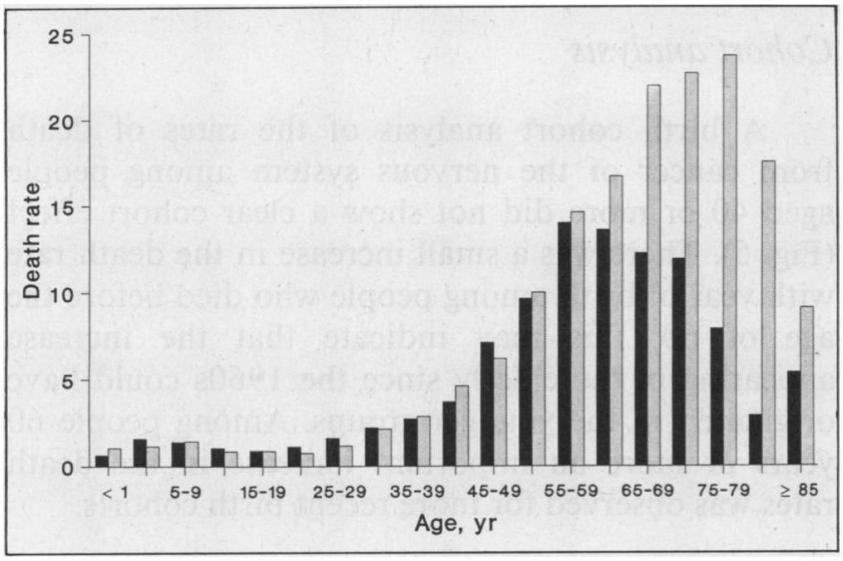


Fig. 1: Age-specific rates of death from brain cancer among males per 100 000 population in Canada from 1965 to 1967 (black bars) and from 1985 to 1987 (screened bars).

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 11| November 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

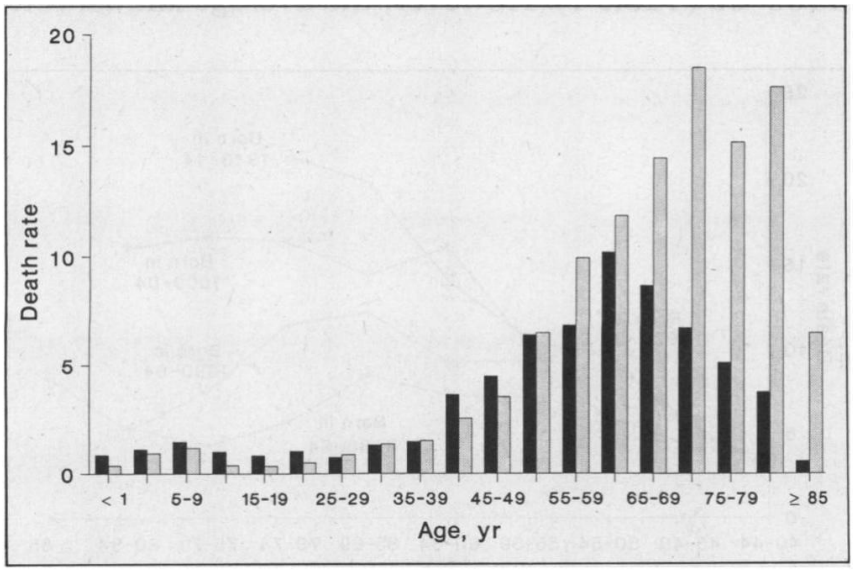


Fig. 2: Age-specific rates of death from brain cancer among females per 100 000 population in Canada. Bar designations as in Fig. 1

- **Age and Sex Distributions**

The age-specific death rates among males and females for two periods are presented in Figs. 1 and 2. During 1965-67 the death rate peaked in the group of people aged 55 to 60 years and then declined. During 1985-87 the death rate increased to a slight peak around age 5 years, decreased until about age 15 to 19, continuously increased until about age 75 to 79 and then decreased. Age patterns were very similar for males and females, although in the two periods the rates among the males were in general slightly higher.[3]

- **Symptoms**
- **General signs and symptoms caused by brain tumors may include:**
  - Headache or pressure in the head that is worse in the morning.
  - Headaches that happen more often and seem more severe.
  - Headaches that are sometimes described as tension headaches or migraines.
  - Nausea or vomiting.
  - Eye problems, such as blurry vision, seeing double or losing sight on the sides of your vision.
  - Losing feeling or movement in an arm or a leg.
  - Trouble with balance.
  - Speech problems.
  - Feeling very tired.
  - Confusion in everyday matters.
  - Memory problems.
  - Having trouble following simple commands.
  - Personality or behavior changes.
  - Seizures, especially if there is no history of seizures.
  - Hearing problems.
  - Dizziness or a sense that the world is spinning, also called vertigo.
  - Feeling very hungry and gaining weight.

Brain tumors that aren't cancerous tend to cause symptoms that develop slowly. Noncancerous brain tumors also are called benign brain tumors. They might cause subtle symptoms that you don't notice at first. The symptoms might get worse over months or years.

Cancerous brain tumors cause symptoms that get worse quickly. Cancerous brain tumors also are called brain cancers or malignant brain tumors. They cause symptoms that come on suddenly. They get worse in a matter of days or weeks.

- **Brain Tumor Headaches**

Headaches are the most common symptom of brain tumors. Headaches happen in about half of people with brain tumors. Headaches can happen if a growing brain tumor presses on healthy cells around it. Or a brain tumor can cause swelling in the brain that increases pressure in the head and leads to a headache.

Headache pain caused by brain tumors is often worse when you wake up in the morning. But it can happen at any time. Some people have headaches that wake them from sleep. Brain tumor headaches tend to cause pain that's worse when coughing or straining. People with brain tumors most often report that the headache feels like a tension headache. Some people say the headache feels like a migraine.

Brain tumors in the back of the head might cause a headache with neck pain. If the brain tumor happens in the front of the head, the headache might feel like eye pain or sinus pain.

- **Causes**
- **Brain tumors that begin in the brain:**

Brain tumors that start as a growth of cells in the brain are called primary brain tumors. They might start right in the brain or in the tissue nearby. Nearby tissue might include the membranes

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 11| November 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

that cover the brain, called meninges. Brain tumors also can happen in nerves, the pituitary gland and the pineal gland.

Brain tumors happen when cells in or near the brain get changes in their DNA. A cell's DNA holds the instructions that tell the cell what to do. The changes tell the cells to grow quickly and continue living when healthy cells would die as part of their natural life cycle. This makes a lot of extra cells in the brain. The cells can form a growth called a tumor.

It's not clear what causes the DNA changes that lead to brain tumors. For many people with brain tumors, the cause is never known. Sometimes parents pass DNA changes to their children. The changes can increase the risk of having a brain tumor. These hereditary brain tumors are rare. If you have a family history of brain tumors, talk about it with your health care provider. You might consider meeting with a health care provider trained in genetics to understand whether your family history increases your risk of having a brain tumor.

When brain tumors happen in children, they're likely to be primary brain tumors. In adults, brain tumors are more likely to be cancer that started somewhere else and spread to the brain.

- **Cancer that spreads to the brain**

Secondary brain tumors happen when cancer starts somewhere else and spreads to the brain. When cancer spreads, it's called metastatic cancer.

Any cancer can spread to the brain, but common types include:

- Breast cancer.
- Colon cancer.
- Kidney cancer.
- Lung cancer.
- Melanoma.

- **Prevention**

There's no way to prevent brain tumors. If you get a brain tumor, you didn't do anything to cause it.
People with an increased risk of brain tumor might consider screening tests. Screening isn't brain tumor prevention. But screening might help find a brain tumor when it's small and treatment is more likely to be successful.

If you have a family history of brain tumor or inherited syndromes that increase the risk of brain tumor, talk about it with your health care provider. You might consider meeting with a genetic counselor or other health care provider trained in genetics. This person can help you understand your risk and ways to manage it. For example, you might consider brain tumor screening tests. Testing might include an imaging test or a neurological exam to test your vision, hearing, balance, coordination and reflexes.

- **Departments and specialties**

Mayo Clinic has one of the largest and most experienced practices in the United States, with campuses in Arizona, Florida and Minnesota. Staff skilled in dozens of specialties work together to ensure quality care and successful recovery.

- **Departments that treat this condition**
  - Brain Metastases Specialty Group
  - Brain Tumor Program
  - Cancer Care at Mayo Clinic
  - Glioma Specialty Group
  - Meningioma Specialty Group
  - Neurology
  - Neurosurgery
  - Oncology (Medical)
  - Pediatric Brain Tumor Clinic
  - Pediatric Hematology/Oncology
  - Pediatric Rehabilitation
  - Physical Medicine and Rehabilitation
  - Proton Beam Therapy Program
  - Radiation Oncology
  - Radiology
  - Skull Base Tumors Specialty Group
  - **Areas that research this condition**
  - Neurologic Surgery
  - Neurology Research
  - Radiology Research

- **Treatment**

Treatment for a brain tumor depends on whether the tumor is a brain cancer or if it's not cancerous, also called a benign brain tumor. Treatment options also depend on the type, size, grade and location of the brain tumor. Options might include surgery, radiation therapy, radiosurgery, chemotherapy and targeted therapy. When considering your treatment options, your health care team also considers your overall health and your preferences.

Treatment might not be needed right away. You might not need treatment right away if your brain tumor is small, isn't cancerous and doesn't cause symptoms. Small, benign brain tumors might not grow or might grow so slowly that they won't ever cause problems. You might have brain MRI scans a few times a year to check for brain tumor growth. If the brain tumor grows more quickly than expected or if you develop symptoms, you might need treatment..

1.Surgery

The goal of surgery for a brain tumor is to remove all of the tumor cells. The tumor can't always be removed completely. When it's possible, the surgeon works to remove as much of the brain tumor as can be done safely. Brain tumor removal surgery can be used to treat brain cancers and benign brain tumors.Some brain tumors are small and easy to separate from surrounding brain tissue. This makes it likely that the tumor will be removed completely. Other brain tumors can't be separated from surrounding tissue. Sometimes a brain tumor is near an important part of the brain. Surgery might be risky in this situation. The surgeon might take out as much of the tumor as

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 11| November 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

is safe. Removing only part of a brain tumor is sometimes called a subtotal resection.

Removal of part of your brain tumor may help reduce your symptoms

2.Radiation Therapy

Radiation therapy for brain tumors uses powerful energy beams to kill tumor cells. The energy can come from X-rays, protons and other sources. Radiation therapy for brain tumors usually comes from a machine outside the body. This is called external beam radiation. Rarely, the radiation can be placed inside the body. This is called brachytherapy.

Radiation therapy can be used to treat brain cancers and benign brain tumors.

External beam radiation therapy is usually done in short daily treatments. A typical treatment plan might involve having radiation treatments five days a week for 2 to 6 weeks.

External beam radiation can focus just on the area of your brain where the tumor is located, or it can be applied to your entire brain. Most people with a brain tumor will have radiation aimed at the area around the tumor. If there are many tumors, the entire brain might need radiation treatment. When all of the brain is treated, it's called whole-brain radiation. Whole-brain radiation is most often used to treat cancer that spreads to the brain from another part of the body and forms multiple tumors in the brain.

Traditionally, radiation therapy uses X-rays, but a newer form of this treatment uses energy from protons. The proton beams can be more carefully targeted to only hurt the tumor cells. They may be less likely to hurt nearby healthy tissue. Proton therapy may be helpful for treating brain tumors in children. It also may help in treating tumors that are very close to important parts of the brain. Proton therapy isn't as widely available as traditional X-ray radiation therapy.

Side effects of radiation therapy for brain tumors depend on the type and dose of radiation you receive. Common side effects that happen during treatment or right after it are fatigue, headaches, memory loss, scalp irritation and hair loss. Sometimes radiation therapy side effects show up many years later. These late side effects might include memory and thinking problems.

3.Radiosurgery

Stereotactic radiosurgery for brain tumors is an intense form of radiation treatment. It aims beams of radiation from many angles at the brain tumor. Each beam isn't very powerful. But the point where the beams meet gets a very large dose of radiation that kills the tumor cells.

Radiosurgery can be used to treat brain cancers and benign brain tumors.

There are different types of technology used in radiosurgery to deliver radiation to treat brain tumors. Some examples include:

- **Linear Accelerator Radiosurgery**

Linear accelerator machines also are called LINAC machines. LINAC machines are known by their brand names, such as CyberKnife, TrueBeam and others. A LINAC machine aims carefully shaped beams of energy one at a time from several different angles. The beams are made of X-rays.

- **Gamma Knife Radiosurgery.**

A Gamma Knife machine aims many small beams of radiation at the same time. The beams are made of gamma rays.

- **Proton Radiosurgery.**

Proton radiosurgery uses beams made of protons. This is the newest type of radiosurgery. It's becoming more common but isn't available at all hospitals.

- **Chemotherapy**

Chemotherapy for brain tumors uses strong medicines to kill tumor cells. Chemotherapy medicines can be taken in pill form or injected into a vein. Sometimes the chemotherapy medicine is placed in the brain tissue during surgery.

Chemotherapy can be used to treat brain cancers and benign brain tumors. Sometimes it's done at the same time as radiation therapy.

Chemotherapy side effects depend on the type and dose of drugs you receive. Chemotherapy can cause nausea, vomiting and hair loss

- **Conclusion**

The case study on brain tumor management in pharmacy highlights the potential of advanced drug delivery systems and innovative therapeutic strategies to overcome significant challenges, such as the blood-brain barrier and drug toxicity. Through the use of targeted therapies like nanoparticles and liposomes, the study demonstrates improved drug efficacy and reduced side effects, offering a promising approach to treating brain tumors. This underscores the critical role of pharmaceutical research in developing effective, patient-centric treatments, paving the way for future clinical applications and advancements in oncology care.

REFERENCE

1. *Brain tumor https://www.mayoclinic.org/diseases-conditions/brain-tumor/symptoms-causes/syc-20350084*
2. *Cancer burden and health systems in India 1 https://scholar.google.com/scholar?hl=en&as_sdt=0%2C5&q=the.+growing+burden+of+cancer+in+india+&btnG=#d=gs_qabs&t=1731752976771&u=%23p%3DLr0J4Cw6w1AJ*
3. *Increasing brain cancer rates in Canada https://pmc.ncbi.nlm.nih.gov/articles/PMC1336078/*
4. *Adult central nervous system tumors treatment (PDQ) – Patient version. National Cancer Institute. https://www.cancer.gov/types/brain/patient/adult-brain-treatment-pdq. Accessed Sept. 27, 2022*
5. *Louis DN, et al. The 2021 WHO classification of tumors of the central nervous system: A summary. Neuro-Oncology. 2021; doi:10.1093/neuonc/noab106*

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 11| November 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

6. *Louis DN, et al. The 2021 WHO classification of tumors of the central nervous system: A summary. Neuro-Oncology. 2021; doi:10.1093/neuonc/noab106.*
7. *Childhood central nervous system germ cell tumors treatment (PDQ) – Patient version. National Cancer Institute. https://www.cancer.gov/types/brain/patient/child-cns-germ-cell-treatment-pdq. Accessed Nov. 15, 2022.*
8. *Stereotactic radiosurgery (SRS) and stereotactic body radiotherapy (SBRT). RadiologyInfo.org.*
9. *https://www.radiologyinfo.org/en/info/stereotactic. Nov. 4, 2022.*
10. *.Klonowicz M., Spych M., Fijuth J. Postoperative radiochemotherapy – a new standard in treatment for glioblastoma? Onkol Prakt Klin. 2007;3:28–31.*
11. *Klonowicz M., Spych M., Fijuth J. Postoperative radiochemotherapy – a new standard in treatment for glioblastoma? Onkol Prakt Klin. 2007;3:28–31.*
12. *Simpson J., Horton J., Scott C. Influence of location and extent of surgical resection on survival of patients with glioblastoma multiforme: results of three consecutive Radiation Therapy Oncology Group (RTOG) clinical trials. Int J Radiat Oncol Biol Phys. 1993;26:239–244. doi: 10.1016/0360-3016(93)90203-8.*
13. *Thomas T., Steward P., Stemhagen A. Risk of astrocytic brain tumors associated with occupational chemical exposures: a case-referent study. Scand J Work Environ Health. 1987;13:417–423. doi: 10.5271/sjweh.2024.*
14. *Thomas T., Steward P., Stemhagen A. Risk of astrocytic brain tumors associated with occupational chemical exposures: a case-referent study. Scand J Work Environ Health. 1987;13:417–423. doi: 10.5271/sjweh.2024.*
15. *Lang F., Miller D., Koslov M. Pathways leading to glioblastoma multiforme. A molecular analysis of genetic alternations in 65 astrocytic tumors. J Neurosurg. 1994;81:427. doi: 10.3171/jns.1994.81.3.0427*