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RESEARCH ARTICLE

Review on Pediatrics Brain

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ABSTRACT

Brain tumors are one of the most devastating diseases faced by modern medicine. 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. Brain tumors are the most common solid tumor among children under 15 year of age. Pediatric brain tumors represent about 20% of all childhood cancers. Two broad types of cancers occurring within this system- Primary tumor originate in the central nervous system, whereas secondary tumors migrate from cancers located elsewhere in the body. Secondary, or metastatic, brain tumors, are more common than primary brain cancers. Brain tumors account for a high percentage of morbidity and mortality in children. It is treated with chemotherapy, radiation therapy and surgery.

Keywords: Pediatric Brain Tumors, Benign, Malignant, Gliomas, Mixed Neuronal-Glial Tumors, Choroid Plexus Papilloma/ Carcinoma, Non- Neuroepithelial Tissue, Meningeal Tumors.

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1. Introduction

Brain tumors are one of the most devastating diseases faced by modern medicine. Brain tumors are primary or metastatic malignancies of the central nervous system with considerable morbidity and mortality. Pediatric brain tumors (PBT) are 15-20% of all brain tumors. Central nervous system (CNS) tumors are the second most common cancer among children.¹ brain tumors are a leading cause of death from childhood cancer, in children up to 19 years of age. Brain tumors are the second leading cause of cancer death in young adults age 20-39.²

Brain:

The brain is a soft, spongy mass of nerve cells and supportive tissue. It is protected by bones of the skull, three thin layers of tissue (meninges) and watery fluid (cerebrospinal fluid) that flows through spaces between the meninges and through spaces (ventricles) within the brain. The human brain is roughly the size of two clenched fists and weighs about 1.5 kilograms. From the outside it looks a bit like a large walnut, with folds and crevices. Brain tissue is made up of about 100 billion nerve cells (neurons) and one trillion supporting cells which stabilize the tissue.

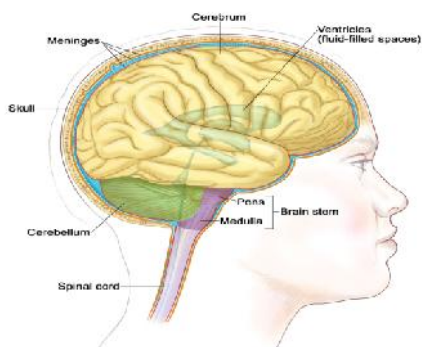


Figure 1: Structure of Brain

The three major parts of the brain control different activities:

Cerebrum:The cerebrum uses information from our senses to tell us what is going on around us and tells our body how to respond. It controls reading, thinking, learning, speech, and emotion. The cerebrum is divided into the left and right cerebral hemispheres. The right hemisphere controls the muscle on the right side of the body.

Cerebellum: The cerebellum controls balance for walking, standing and other complex action.

Brain stem:

The brain stem connects the brain with the spinal cord. It controls breathing, body temperature, blood pressure and other basic body functions.² The brain and spinal cord from the central nervous system this complex system 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.³

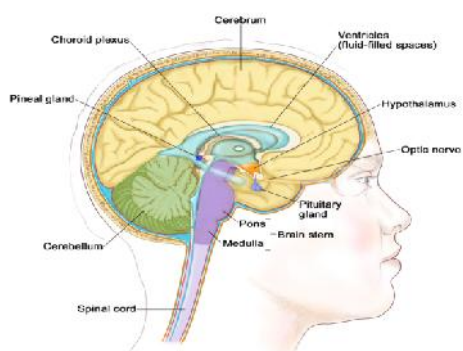


Figure 2: Inside structure of brain

Cancer:

Cancer is defined as unregulated growth of abnormal cells. Abnormal cells that grow into/around parts of the body and interfere with their normal functioning. Spread to distant organs in the body. It is known medically as a malignant neoplasm.

Epidemiology:

Brain tumors are the most common solid tumor among children under 15 years of age. Pediatric brain tumor represent about 20% of all childhood cancer.⁴ More than 50,000 children are affected due to brain disorders. Childhood brain tumors account for a small percentage of all primary brain tumors (adults + children) but brain

tumors account for a high percentage of morbidity and mortality in children.⁵ Brain tumors are a leading cause of death from childhood cancer, in children up to 19 years of age. Brain tumors are the second leading cause of cancer death in young adults age 20-39.

Types of tumors:

The cancer may also spread to more distant parts of the body through the lymphatic system or blood stream. All tumors are not cancerous. Benign tumors do not grow uncontrollably, do not invade neighboring tissues, and do not spread through the body.

Table 1: Difference between benign and malignant tumor

Benign	Malignant
Benign brain tumors do not contain cancer cells	Malignant brain tumors contain cancer cells.
Do not spread throughout the body	Malignant brain tumor very rarely spread to other areas of the body, they can spread throughout the brain or to the spine.
Typically have clear borders	They do not have clear borders.
It grows slowly	Life-threatening because they grow rapidly and invade surrounding brain tissue.
Tumors can be removed entirely, they tend not to return	These tumors can be treated with surgery, chemotherapy and radiation, but they may recur after treatment.

Brain cancer:

A brain tumor is an abnormal growth of tissue in the brain or central spine that can disrupt proper brain function. All brain tumors can grow to damage areas of normal brain tissue if left untreated, which could be disabling and possibly fatal. Brain and spinal cord tumors are different for everyone. They form in different areas, develop from different cell types, and may have different treatment options., both low grade (benign) and high grade (malignant) brain tumors. There are over 120 types of brain and central nervous system tumors.

Primary: Whether cancerous or benign, tumors that start in cells of the brain are called primary brain tumors. Primary brain tumors may spread to other part of the brain or to the spine, but rarely to other organs. Primary tumor type are - 16% glioblastoma, 7% astrocytoma, 35% meningioma, 14% pituitary, 9% nerve sheath, 2% lymphoma, 33% other (Ependymoma, Oligodendroglioma, Embryonal, etc.)

Metastatic or Secondary: Metastatic or secondary brain tumors begin in another part of the body and then spread to the brain. These tumors are more common than primary brain tumors and are named by the location in which they begin. They are treated based on where they originate, such as the lung, breast, colon or skin.

Commonly occur pediatrics brain tumors

Gliomas:

The most common type of brain tumor at all ages is a glioma. Glioma consist of glial cells, which from the

supportive tissue of the brain. The major types of glial tumors are astrocytomas, medulloblastomas, brainstem gliomas and ependymomas.

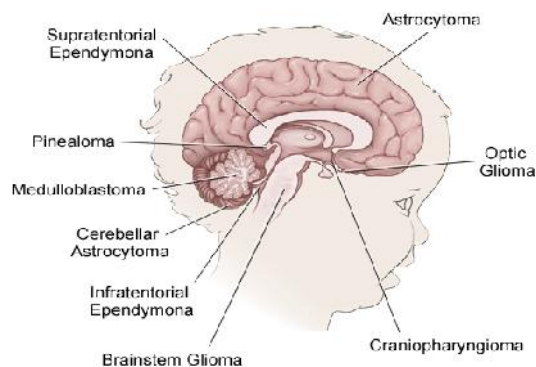


Figure 3: Location of different types of brain tumor

Astrocytomas are usually noncancerous, slow-growing tumors. They commonly develop in children age 5 to 8. Also called low-grade gliomas, these are the most common brain tumors in children.

Medulloblastomas are the most common type of childhood brain cancer. Most medulloblastomas occur before age of 10 years.

Ependymomas are a type of childhood brain tumor that can be benign (non-cancerous) or malignant (cancerous). The location and type of ependymoma determine the type of therapy needed to control the tumor.

Brainstem Gliomas are very rare tumors that occur almost only in children. The average age at which they develop is about 6. The tumor may grow very large before causing symptoms.

Mixed Neuronal- Glial Tumors:

Tumors containing a mix of glial cells (most commonly astrocytes) and neuron (ganglion cells) occur more often in children than in adults. They may develop anywhere in the nervous system but most typically appear in the cerebrum, an area of the brain involved in motor function and personality. Surgery to remove mixed neuronal-glioma tumors is often effective.

Ganglioglioma is the most common of the mixed neuronal-glioma tumors and generally appears in childhood or the early teen years. The majority are benign and can usually be treated successfully by surgery.

Subependymal giant cell tumors are common in children who have a genetic condition called tuberous sclerosis. These tumors are rarely malignant.

Pleomorphic xanthoastrocytoma tumors are most commonly seen in teens or young adults; most are benign.

Embryonal Tumors: Up to 25% of nervous system tumors that occur in infants and children are tumors made up of poorly differentiated cells into glial (supportive tissue) and nerve cells. When the nervous system develops, neuroepithelial cells are those that differentiate into glial (supportive tissue) and nerve cells. The two main types of embryonal tumors are:

Primitive neuroectodermal tumors (PNET) are most common embryonal tumor can arise anywhere in the

nervous system but typically appears in the cerebellum. New advances in therapy have made treatment more effective for these tumors.

Atypical teratoid/ rhabdoid tumor are 90% of patients with these tumors are age 2 or younger. Approximately 90% of these tumors have a chromosomal abnormality involving chromosome 22. These tumors may arise anywhere in the nervous system but typically appear in the cerebellum. They may also appear in the kidneys of infants. At the time of diagnosis, about one-third of these tumors have spread throughout the nervous system.

Choroid Plexus Papilloma/ Carcinoma:

These tumors may also be found in ventricles. They may be benign or malignant, and may spread throughout the nervous system. Choroid plexus papillomas/ carcinomas are filled with blood vessels (vascular), making them difficult to remove because of their tendency to bleed.

Tumors Arising From Non- Neuroepithelial Tissue:

The intracranial (inside the skull) and intraspinal (within the spine) cavities contain tissues and structures that may give rise to tumors, a number of which are more common in children than adults. These tumors include:

Craniopharyngioma are benign tumors. These are thought to originate from residual tissue left behind following the development of the head. Because they occur at the front base of the brain near the pituitary gland and optic nerves, they may cause serious neurological and endocrine problems. Surgery may not be able to completely remove them.

Pineal region tumors arise near the pineal gland at the base of the skull. The most common type is **Germinoma**. It is treated with radiation.

Meningeal Tumors:

The brain and spinal cord are covered with membranes called dura mater, arachnoid and pia mater. Tumors called meningiomas may develop in these membranes, but are more common in adults than children.

Tumor Grading:

The World Health Organization (WHO) has created a standard by which all tumors are classified. Tumors are given a name based on the cells where they arise, and a number ranging from 1-4, usually represented by Roman numerals I-IV. This number is called the "grade" and it represents how fast the cells can grow and are likely to spread. This is critical information for planning treatment and predicting outcomes. Lower grade tumors (grades I & II) are not very aggressive and are usually associated with long-term survival. Higher grade tumors (grade III & IV) grow more quickly, can cause more damage, and are often more difficult to treat. These are considered malignant or cancerous.⁶

Types of Tumors

Grade –I Tumor:

- Slow-growing cells
- Almost normal appearance under a microscope
- Usually not cancer
- Associated with long-term survival
- Can potentially be cured with surgery

Grade –II Tumor:

- Relatively slow-growing cells
- Slightly abnormal appearance under a microscope
- Can invade adjacent normal tissue
- Can recur as a higher grade tumor

Grade –III Tumor:

- Actively reproducing abnormal cells
- Abnormal appearance under a microscope
- Infiltrate adjacent normal brain tissue
- Tumor tends to recur, often as a higher grade

Grade –IV Tumor:

- Abnormal cells which reproduce rapidly
- Very abnormal appearance under a microscope
- From new blood vessels to maintain rapid growth
- Areas of dead cells (necrosis) in center

Tumors can contain several grades of cells; however, the most malignant cell determines the grade for the entire tumor (even if most of the tumor is a lower grade). Some tumors can change the way they grow and may become malignant over time.

Symptoms of Brain Tumors:

A brain tumor can block the flow of cerebrospinal fluid (CSF) between the ventricles, causing a buildup of CSF and swelling, called brain edema. Edema can lead to symptoms including headaches, which can be most severe in the morning, seizures or focal deficits. A tumor of the spinal cord can block the communication between the brain and nerves throughout the body. Focal deficits include damage to sensory or movement abilities, problem in the ability to process information, personality changes, and speech disorders. This can lead to problems with movement or physical sensation like weakness or paralysis in one part or one side of the body, vision changes, nausea or vomiting, confusion and disorientation.

Diagnosis:

Cancer can be detected in a number of ways, including the presence of certain signs and symptoms, screening tests, or medical imaging.

Infants may have the following physical signs:

- No red reflex in the eye
- Positive Babinski reflex
- Enlarge eyes
- Bulging fontanelle

The following tests may be used to detect a brain tumor and identify its location:

Computerized tomography scan (CAT scan or CT scan)- This imaging procedure uses a combination of X-ray and computer technology to produce cross-sectional images (called 'slices') both horizontal and vertical of the bones, muscles, fat and organs.

Magnetic resonance images (MRI)- This imaging procedure uses a combination of large magnets, radiofrequencies and a computer to produce detailed images of organs and structures within the body.

X – ray –This imaging test uses invisible electromagnetic energy beams to produce images of internal tissues, bone and organs onto film.

Angiogram – This imaging test uses a dye to visualize all the blood vessels in the brain to detect certain types of tumors.

Lumbar puncture / spinal tap – A special needle is placed into the lower back and into the spinal canal around the spinal cord. A small amount of cerebrospinal fluid, which surrounds the brain and spinal cord, can be removed and sent for testing.

Surgery biopsy – A surgical procedure to remove a small of tissue from the tumor so the cells can be examined under a microscope.⁷

Treatment:

Cancer is usually treated with chemotherapy, radiation therapy and surgery.⁸ Treatment decisions are based on the tumor type, tumor location, symptoms and the patient's age. In selected cases, tumor surveillance by repeated magnetic resonance imaging (MRI) can be justified.⁹ The histopathology diagnosis is the foundation for further treatment decisions, together with tumor location, tumor stage, result of surgery, and the patient's age.

The nonmalignant tumors (WHO grade I - II) after surgery no further treatment is usually required, although exceptions to this rule exist. The malignant tumors (WHO grade III –IV) cannot be cured by surgery alone, even if a complete resection is achieved. Therefore they are treated with surgery together with chemotherapy and /or radiotherapy.¹⁰

2. 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. Pediatric brain tumor represents about 20% of all childhood cancer. More than 50,000 children are affected due to brain disorders. Recent advances in treating brain tumors with limited surgery, radio-surgery, and controlled toxicities have decreased the morbidity and improved the access and acceptance of pediatric patients to brain tumor therapy. Clinical trials are needed that are designed specifically for the treatment of brain tumors in the pediatrics.

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