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Research article

Brain Tumor in Children

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Abstract

Brain tumor in children is a disease in which abnormal cells are formed in the brain tissues. There are many types of brain tumors in childhood. Tumors can be benign or malignant. Benign brain tumors grow and press on nearby areas of the brain. They rarely spread to other organs.

Keywords: PChild; Brain; Tumor; CNS

Introduction

Nervous system tumors may be primary or secondary tumors of the central nervous system (CNS), which includes the brain and spinal cord [1]. They are classified according to their cell of origin and graded according to their malignant behavior. Although histologically the tumor may be benign, the enclosed nature of the CNS may result in tumor effects causing significant damage or even death. Among children, brain tumors are the most frequent cause of solid tumor cancer–related deaths. Incidence and mortality rates are highest among whites and men. Among children, there has been a slight rise in incidence and a decrease in mortality in the past 30 years. There are relatively few known risk factors for brain and CNS cancers. Patients with exposure to radiation and vinyl chloride and those with certain genetic syndromes may be at higher risk. The primary CNS tumor may be diagnosed because of symptoms related to changes in functions of neurons, spinal cord or brain compression, or symptoms resulting from obstruction of the flow of cerebrospinal fluid (e.g., increased intracranial pressure). Surgery, radiation, and chemotherapy are commonly used treatments, while biologic therapy and hyperthermia therapy are being explored through clinical trials.

The headache of a brain tumor is intermittent initially but very quickly increases in frequency and severity [2]. It is often present in the very early-morning hours and may awaken the child from sleep, as lying supine slows the drainage of CSF, increasing ICP. There may be associated projectile vomiting in the absence of nausea. Localization may be difficult, especially in the case of midline lesions. Occipital headache may indicate a posterior fossa lesion, although the pain is frequently referred to a frontotemporal location. Thus, frontal headache may accompany either a supratentorial or a posterior fossa tumor. Pediatric headache is a common health problem in children, with a significant headache reported in more than 75% by the age of 15 years [3]. In approximately 50% of patients with migraines, the headache disorder starts before the age of 20 years. In the US, adolescent boys and girls have a headache prevalence of 56 and 74%, and a migraine prevalence of 3.8 and 6.6%, respectively. A small percentage of headaches in children are secondary in nature. A primary concern in children with headache is the possibility of a brain tumor. Although brain tumors constitute the largest group of solid neoplasms in children and are second only to leukemia in overall frequency of childhood cancers, the annual incidence is low at 3 in 100,000. Primary brain neoplasms are far more prevalent in children than they are in adults. They account for almost 20% of all cancers in children but only 1% of cancers in adults. Central nervous system tumors are the second cause of cancer-related deaths in patients younger than 15 years.

Normal Growth

In this growing age of managed care and required medical referrals, it is increasingly likely that children and adolescents will present to primary care settings with concerns related to developmental delay in one or more of their developmental domains as well as general medical issues that may have implications for adaptive functioning [4]. While schools must provide assessment of youth with neurodevelopmental disabilities (as early as age 3 years), the schools have strict guidelines for implementing an Individual Education Plan (IEP). The process usually cannot be

completed in a timely manner or the school is unable to provide the type of assessment required (i.e., intellectual, neurodevelopmental, neuropsychological, behavioral, and psychosocial) to address the medical referral question. Youth identified early in life with developmental risks or concerns are often referred to early intervention programs (varying in title by state) to monitor, track, and ensure engagement with appropriate services prior to the time that public educational settings would take over. It may even be the case that youth across the age span with various medical conditions (e.g., head injury, spina bifida, cerebral palsy, diabetes, metabolic conditions, chronic illness, physical disabilities, and brain tumors) are often referred for psychological assessment via primary or specialty care, long before the academic process is involved. Youth who have non-specific delays combined with average to above average intellectual function are often able to adapt to their environments well enough to mitigate significant maturational, academic, social, or emotional deficits until they reach situations that require higher order functioning (e.g., fourth grade academic demands, entering middle school or high school). In order to better understand the concept of assessment, a discussion related to "normal" neurodevelopment or "normal" development will be helpful.

Neurodevelopment in a broad sense refers to the growth and maturation of the nervous system, as well as sensory and perceptual abilities of the child. Normal growth and development is characterized by individual variations in the rate of progression and achievement of milestones and the sequential nature of this progression. Although largely determined by genetic factors, environmental factors (such as opportunity, nutrition, and social context) also play a significant role in overall development of a child or adolescent. Capute noted that motor milestones are mostly influenced by maturation of the neurological system; on the other hand, social and adaptive skills are influenced largely by environmental factors, such as social expectations, education, and training. The term neurodevelopment encompasses various domains which can be broadly categorized as physical or somatic, neurological, sensory-perceptual, cognitive, and psychosocial or emotional.

Malignancies

In children from 1 to 19 years of age, malignancies are the leading cause of natural death in the USA [5]. Although sudden unexpected death in children due to malignancies is exceedingly rare, it does occur, and those cases are likely to come to the attention of the forensic pathologist. In such cases, sudden death generally occurs due to direct involvement of vital structures including primary-cardiac or central nervous system tumors or sequelae such as hemorrhage secondary to leukemia or lymphoma. A number of case studies have been published documenting sudden death in children with undiagnosed brain tumors (primarily glioblastomas) and leukemia and lymphoma. Sudden deaths in children have also resulted from tumor emboli, pulmonary emboli, and hemorrhage due to underlying malignancies. Childhood brain tumors are associated with a number of genetic syndromes that include neurofibromatosis type I (associated with low-grade optic tract gliomas and other brain tumors) and type 2 (associated with acoustic neuromas), tuberous sclerosis (associated with CNS tubers and subependymal giant-cell astrocytomas), von Hippel-Lindau disease (associated with hemangioglioblastomas), and familial cancer predisposition syndromes (e.g., Li-Fraumeni syndrome associated with choroid plexus carcinomas). Presenting symptoms in children with primary brain tumors include headaches, increased intracranial pressure, vomiting, and seizures. Most children with brain tumors who present with headaches also commonly experience vomiting and will have increased intracranial pressure and obstructive hydrocephalus. Low-grade tumors of the cerebral cortex may cause seizures, and as previously discussed, seizures can be a cause of sudden death in children.

Symptoms [6]:

a) 60% infratentorial (cerebellum, brain stem).

b) 40% supratentorial (cerebral hemispheres, thalamus).

Associated:

a) Neurofibromatosis Types I & II

b) Tuberous sclerosis

c) Von Hippel-Lindau

d) Ataxia-telangectasia

e) Gorlin

f) Li-Fraumeni

g) Astrocytoma, medulloblastema associated w/ p53 mutation

Increased ICP:

a) Headache

b) AM vomiting

c) Impaired vision: Blurriness (papilledema) Diplopia (CN VI palsy)

d) Lethargy

e) School performance & personality changes

f) Ataxia

g) Focal seizures

Infants:

a) Anorexia

b) Irritability

c) Increasing head circumference

d) Failure to thrive

e) Loss of milestones (developmental delay)

Diagnosis [6]:

Cerebral hemisphere:

a) Astrocytoma

b) Ependymoma

c) Glioblastoma

d) Meningioma

Sella/chiasm:

a) Craniopharyngioma

b) Pituitary adenoma

c) Optic nerve glioma

Cerebellum:

a) Medulloblastoma

b) Astrocytoma

c) Meningioma

Brain stem:

a) Astrocytoma

b) Ependymoma

c) Glioblastoma

d) Cerebral hemorrhage

e) Head trauma: cerebral contusion

Prognosis

Brain tumors can cause symptoms by impingement on normal tissue (usually cranial nerves) or by an increase in intracranial pressure caused either by obstruction of cerebrospinal fluid (CSF) flow or by a direct mass effect [7]. Tumors that obstruct the flow of CSF quickly become symptomatic. In young children with open cranial sutures, an increase in head circumference may occur. Optic pathway tumors may lead to loss of visual acuity or visual field defects. Inability to abduct the eye as the result of sixth cranial nerve palsy is a common sign of increased intracranial pressure. Other cranial nerve deficits suggest involvement of the brainstem. Seizures occur in 20-50% of patients with supratentorial tumors; focal weakness or sensory changes also may be seen. Pituitary involvement can produce neuroendocrine effects such as precocious puberty or diabetes insipidus. Cerebellar tumors are associated with ataxia and diminished coordination. A history and physical examination are fundamental for evaluation and should include a careful neurological assessment, including visual fields and a funduscopic examination. The classic triad of morning headache, vomiting, and papilledema is present in fewer than 30% of children at presentation [7]. School failure and personality changes are more common in older children while irritability, failure to thrive, and delayed development are common in very young children with brain tumors. Recent-onset head tilt can result from a posterior fossa tumor.

Brain tumors are the most common solid tumors of childhood, accounting for 1500–2000 new malignancies in children each year in the United States and for 25%–30% of all childhood cancers. In general, children with brain tumors have a better prognosis than do adults. Favorable outcome occurs most commonly with low-grade and fully resectable tumors as well as with chemoradiation responsive tumors such as medulloblastoma. Unfortunately, cranial irradiation in young children can have significant neuropsychological, intellectual, and endocrinologic sequelae. Brain tumors in childhood are biologically and histologically heterogeneous, ranging from low-grade localized lesions to high-grade tumors with neuraxis dissemination. High-dose systemic chemotherapy is used frequently, especially in young children with high-grade tumors, in an effort to delay, decrease, or completely avoid cranial irradiation. Such intensive treatment may be accompanied by autologous HSCT (hematopoietic stem cell transplant) or peripheral stem cell reconstitution.

Child's Age

Childhood brain tumors occur most frequently in the posterior fossa [8]. The most common tumors are medullo blastoma, brainstem glioma, ependymoma, and cystic astrocytoma. There are 3 potential areas of involvement: cranial nerves, pyramidal tracts, and the cerebellum. Although symptoms may be reported to have developed over the course of days, a careful history typically reveals subtle signs of weakness and coordination difficulties lasting weeks to months. Signs from obstruction of cerebrospinal fluid (CSF) flow are common, and children younger than 2 years typically present with increasing head circumference. In older children, symptoms such as headaches and ataxia are more common. The average time from symptom onset to diagnosis is 7 months. Although less common than brain tumors, spinal tumors can also present with ataxia. Depending on the spinal level, signs of weakness or sensory loss referable to the lower or upper extremities with preservation of reflexes will be present. In addition, paraneoplastic presentation of tumors (eg, opsoclonus–myoclonus syndrome) at times need to be considered in the differential diagnosis of ataxia.

Clinical findings at presentation vary depending on the child's age and the tumor's location [9]. Children younger than 2 years more commonly have infratentorial tumors. Children with such tumors usually present with nonspecific symptoms such as vomiting, unsteadiness, lethargy, and irritability. Signs may be surprisingly few or may include macrocephaly, ataxia, hyperreflexia, and cranial nerve palsies. Because the head can expand in young children, papilledema is often absent. Measuring head circumference and observing gait are essential in evaluating a child for possible brain tumor. Eye findings and apparent visual disturbances such as difficulty tracking can occur in association with optic pathway

tumors such as optic glioma. Optic glioma occurring in a young child is often associated with neurofibromatosis. Older children more commonly have supratentorial tumors, which are associated with headache, visual symptoms, seizures, and focal neurologic deficits. Initial presenting features are often nonspecific. School failure and personality changes are common. Vaguely described visual disturbance is often present, but the child must be directly asked. Headaches are common, but they often will not be predominantly in the morning. The headaches may be confused with migraine.

Emergency Department

Headaches can be caused by mass effect from a pathologic lesion that produces traction and/or compression involving pain-sensitive structures of the head and neck [10]. For the emergency physician, the most important conditions in this category are intracranial hemorrhage and brain tumor. An intracranial hemorrhage produces displacement of surrounding tissues and, in cases of more significant bleeding, increased ICP. In the pediatric population, this is most often the result of a severe head injury. However, in rare instances, a child can have a nontraumatic intracranial hemorrhage from a ruptured vascular anomaly (e.g., an arteriovenous malformation), which leads to bleeding into the brain parenchyma and ventricles. As with other vascular events, this type of hemorrhage is characterized by the abrupt onset of severe pain. In contrast, headaches resulting from a brain tumor typically have a more insidious onset. The child will often complain of progressively worsening headaches for several weeks or even months. Additional symptoms, such as persistent vomiting or gait abnormalities, may also be present. Unfortunately, the physical examination can be normal during the early phase of the illness, and as mentioned previously, this commonly leads to a delayed diagnosis. Other processes that cause headache as a result of traction and compression include idiopathic intracranial hypertension (pseudotumor cerebri), brain abscess, hydrocephalus, and persistent spinal fluid leak after lumbar puncture.

The diagnosis for pediatric patients presenting with headache will be evident in all but a small minority of cases after a thorough history and physical examination. Laboratory tests and imaging modalities are rarely needed. Even if a definitive diagnosis cannot be established immediately, the identification of a potentially life-threatening cause of headaches will almost always be possible before the child leaves the ED. Concern about the possibility of a more serious cause warrants aggressive use of whatever diagnostic or therapeutic interventions are indicated, such as a computed tomography (CT) scan of the head, lumbar puncture, or intravenous antibiotics. Occasionally, a child with a suspected brain tumor will be appropriately discharged from the ED without undergoing any diagnostic tests. Such a disposition assumes that proper follow-up for such patients can be arranged and that magnetic resonance imaging (MRI) of the head will be performed within 24 to 48 hours.

Management

Therapy for brain tumors includes a combination of surgery, radiation, and chemotherapy, depending on the location and extent of the tumor [11]. Because they are located so deeply, most tumors cannot be completely removed in children; this makes radiation and chemotherapy increasingly important. Radiation therapy may be intense because, if tumor tissue is not rapidly proliferating, cells are not easily destroyed. Chemotherapy is limited because many chemotherapeutic agents do not cross the blood–brain barrier. Administration of a drug directly into the ventricular system via a reservoir (Ommaya) may increase drug effectiveness. Research is revealing special gene activating factors found in children's brain tumors that will serve as a basis for future therapy. The diagnosis of brain tumor at any age is always a serious one and a stress for parents. Closely observe a child who is admitted to the hospital for a possible diagnosis of brain tumor, to detect signs of increased intracranial pressure or new localizing signs as they occur. Record pulse rate, blood pressure, and respiratory rate with extreme accuracy, so that subtle changes become apparent. Note and document episodes of irritability, drowsiness, speech difficulty, and eye involvement. Statements such as, "Child says he sees two forks when I show him one" or "Child is unable to see objects held in her left field of vision" are much more meaningful to a neurosurgeon than "Child has difficulty seeing." Completely describe any seizure activity observed, particularly the beginning movements of the seizure, because these may help to localize the point of maximum brain pressure. Side rails should be in place for protection in case a seizure occurs while the child is in bed.

Conclusion

Although tumor is rare in children, brain tumors are the third most common type of tumor in childhood, after leukemia and lymphoma. Approximately 35 cases of brain tumors are diagnosed per 1.000.000 children under the age of 15 per year. They most often occur between the ages of 3 and 7. Most brain tumors (60-70%) originate from glial cells and do not tend to metastasize outside the CNS. The causes of many types of brain tumors in childhood are not known.

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