

Diagnosis and Treatment of Pediatric Brain Tumors

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Abstract

Objective. Tumors of the brain and spine make up about 20% of all childhood cancers; they are the second most common form of childhood cancer after leukemia. Brain tumors are the most common solid tumor in children. Symptoms depend on a variety of factors, including location of the tumor, age of child, and rate of tumor growth. The aim of study was to present our experience with the diagnosis and treatment of brain tumors in children. **Patients and Methods.** The aim of this study is to analyze clinicopathological characteristics, treatments, complications, and outcomes in children with brain tumors. This study is a retrospective analysis of 27 consecutive patients younger than 16 years and hospitalized for surgical treatment of brain tumors. Intracranial hypertension, neurological status, radiological computerized tomography (CT) or magnetic resonance imaging (MRI) findings, tumor localization, type of resection, hydrocephalus treatment, histopathology, complications, and outcome were analyzed. **Results.** Twenty-seven surgeries were performed in patients for brain tumors. There were 9 females and 18 males. The average patient age was 7.8 years. There were 11 (40%) children with astrocytoma; of these, there were 9 (82%) pilocytic astrocytomas and 2 (18%) ordinary histopathological subtypes of high-grade tumors. **Conclusion.** As with any cancer, prognosis and long-term survival vary greatly from child to child. Prompt medical attention and aggressive therapy are important for the best prognosis. Continuous follow-up care is essential for a child diagnosed with a brain tumor.

Key Words: Pediatric Brain Tumors ▪ Diagnosis ▪ Treatment.

Introduction

Tumors of the nervous system represent a diverse spectrum of underlying molecular biological subtypes, prognostic categories, age distribution, and treatment recommendations. Pediatric central nervous system tumors are the most common solid tumors in children and are the leading cause of cancer-related morbidity and mortality. Among all childhood cancers, brain tumors are second only to leukemias in incidence (20%) and are the most common solid pediatric tumor (1), comprising 40–50% of all tumors (2). The annual incidence is 2–5 cases per 100,000 children. The most common pediatric brain tumors are gliomas (cerebellum, brain stem, and optic nerve), pineal tumors, craniopharyngiomas, teratomas, granulomas, and

primitive neuroectodermal tumors (PNETs; primarily medulloblastomas) (3).

Signs and symptoms depend on a variety of factors, including the location of the tumor, age of child, and rate of tumor growth. It has traditionally been taught that most pediatric brain tumors (60%) are infratentorial, and that these are equally divided among brain stem gliomas, cerebellar astrocytomas, and medulloblastomas. In reality, the ratio of supratentorial to infratentorial tumors is dependent on the specific age group studied. Supratentorial tumors are more common in infants and children up to 3 years of age and again after age 10, while infratentorial tumors are more common between the ages of 4 and 10 (4). Younger children have a higher incidence of tumors of em-

bryonal origin, whereas older patients tend to have tumors of glial origin. Astrocytomas are the most common supratentorial tumor in pediatrics as in adulthood.

The goal of this study was to present our experience with the diagnosis and treatment of pediatric brain tumors. Also, we discuss the presentation, localization, histology, therapy, and outcome of 2 pediatric brain tumor cases.

Patients and Methods

We completed a database search for records over an 8-year period and identified 27 patients who were surgically treated for pediatric brain tumors. Tumor diagnosis was confirmed at surgery—all cases were included in this study. Demographic, clinical, radiological, and operative data of this patient population were reviewed from the hospital charts and a computerized data bank. In addition, we describe outcome and follow up after discharge from the hospital.

Each brain tumor patient was evaluated by pediatricians, radiologists, neurosurgeons, and oncologists. Clinical findings and ultrasound investigation, computerized tomography (CT), and/or magnetic resonance imaging (MRI) scans of the spine and head were done during diagnosis and at follow-up. Tumor size, anatomical location, and histopathology results were noted. Associated

conditions (such as large head size, suggesting underlying hydrocephalus), comorbidity, and associated congenital anomalies were also noted. Detailed neurological examination was performed, noting specifically the presence or absence of any neurological deficit.

Surgical treatment for brain tumor included craniotomy for tumor removal when possible. Depending upon the anatomical location of the tumor, either complete resection or partial resection was done. The goal of surgery was to remove the tumor with preservation of brain function and without neurological deficit.

Results

The neurosurgical data of 27 patients with brain tumor who were admitted over the 8-year period and treated in the Department of Neurosurgery of our institution were retrospectively studied. There were 9 females and 18 males (ratio, 1:2). The average age at the time of presentation was 7.8 years, ranging from 6 months to 16 years. The most common tumor types by localization are shown in Table 1. The most frequent tumor was pilocytic astrocytoma in 9 cases (34%), followed by craniopharyngioma in 4 cases (15%), and ganglioglioma in 4 cases (15%). Patient's characteristics and treatment modalities are shown in Table 2. There was no surgical mortality in this study.

Table 1. Type of Pediatric Brain Tumors

| Type of Tumor | Infratentorial (N) | Supratentorial (N) | Total, N (%) |
|--------------------------|--------------------|--------------------|--------------|
| Pilocytic astrocytoma | 7 | 2 | 9 (34) |
| Craniopharyngioma | - | 4 | 4 (15) |
| Ganglioglioma | - | 4 | 4 (15) |
| Medulloblastoma | 3 | - | 3 (11) |
| PNET | 2 | - | 2 (7) |
| Astrocytoma gr. II | 2 | - | 2 (7) |
| Hemangioma | 2 | - | 2 (7) |
| Choroid plexus carcinoma | - | 1 | 1 (4) |
| Total | 16 | 11 | 27 (100) |

PNET=Primitive neuroectodermal tumor.

Table 2. Characteristics of Patients and Treatment Modalities

| Type of tumor | Age (yrs) | Sex, M/F | Type of resection Total/Subtotal | Adjuvant therapy |
|--------------------------|-----------|----------|-------------------------------------|-------------------|
| Pilocytic astrocytoma | 10.5 | 7/2 | 8/1 | - |
| Craniopharyngeoma | 6.2 | 2/2 | 3/1 | Radiotherapy |
| Ganglioglioma | 4.1 | 3/1 | 3/1 | - |
| Medulloblastoma | 7.1 | 2/1 | 2/0 | Radiochemotherapy |
| PNET | 11.4 | 1/1 | 2/0 | - |
| Astrocytoma gr. II | 12.2 | 1/1 | 1/1 | - |
| Hemangioma | 7.3 | 1/1 | 2/0 | - |
| Choroid plexus carcinoma | 3.8 | 1/0 | 1/0 | Radiochemotherapy |

PNET=Primitive neuroectodermal tumor.

Case 1

A previously healthy 13-year-old girl with adequate neuropsychomotor development was admitted to the hospital with a 10-day-long history of headache, vomiting, and deteriorating consciousness. Skull CT and MRI scans showed a deep-seated, irregularly shaped, mural and cystic, expansive and compressive lesion in the right cerebellar hemisphere with contrast uptake that was imping-

ing on and obstructing cerebrospinal fluid (CSF) pathways (Figure 1). A craniotomy with total tumor removal was performed. The histopathology characteristics of the tumor showed a pilocytic astrocytoma. The patient's level of consciousness improved after surgery and her symptoms disappeared. The patient was discharged 8 days after the procedure without neurological deficit. Postoperative MRI showed satisfactory result without tumor remnant (Figure 2).

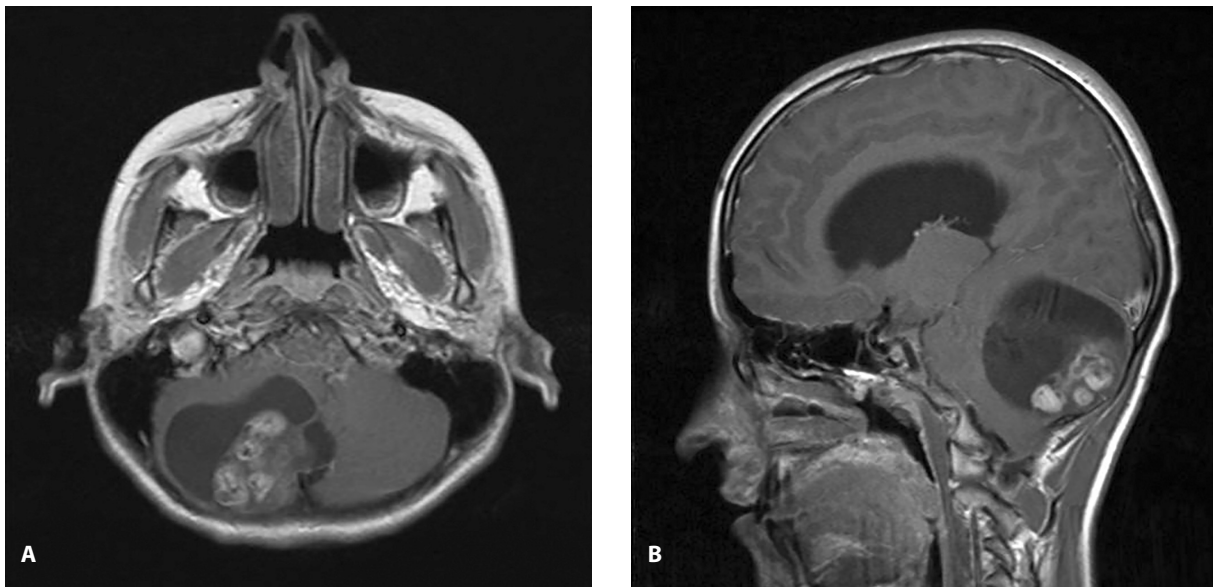


Figure 1. Axial (A) and sagittal (B) MRI showing irregularly shaped, mural and cystic, expansive and compressive lesion in the right cerebellar hemisphere with contrast uptake (pilocytic astrocytoma).

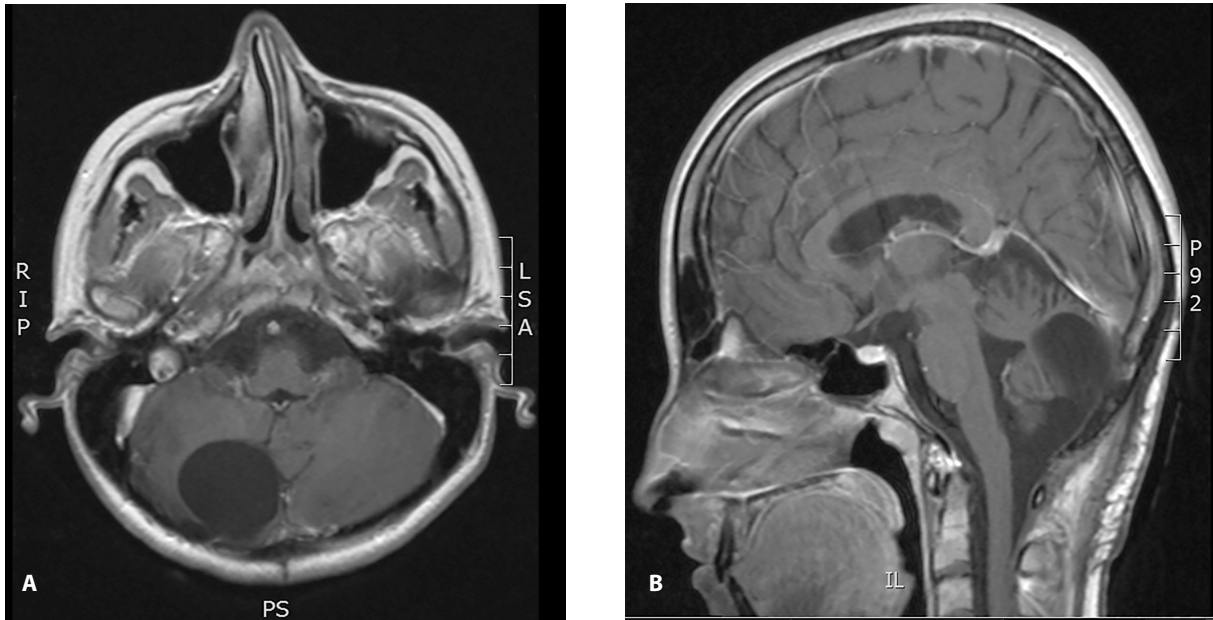


Figure 2. Postoperative axial (A) and sagittal (B) MRI without tumor remnant.

Case 2

A previously healthy 10-year-old boy was admitted to the hospital with a 20-day-long history of headache and vomiting, as well as seizure on the day of admission to the hospital. A skull CT and MRI scans showed a deep-seated, irregularly round, expansive, and compressive brain lesion in the right temporo-occipital region with contrast

uptake (Figure 3). A right temporo-occipital craniotomy with total tumor removal was performed. The histopathology characteristics of the tumor showed a ganglioglioma. The patient's symptoms disappeared, and the patient was discharged 8 days after surgery without neurological deficit. Postoperative MRI showed satisfactory resolution without tumor remnant (Figure 4) and the patient had good seizure control.

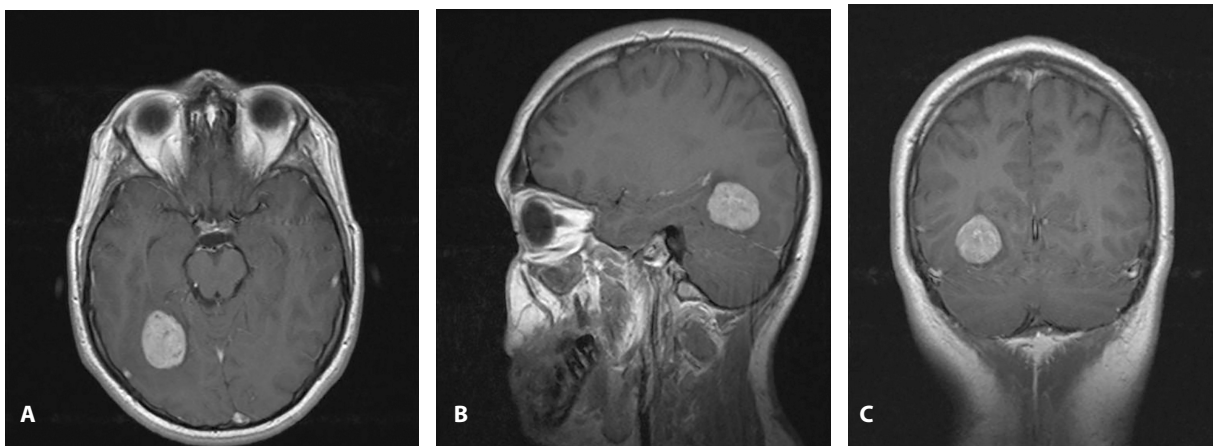


Figure 3. Axial (A), sagittal (B), and coronal (C) MRI showing irregularly round solid expansive and compressive brain lesion in the right temporo-occipital region with contrast uptake (ganglioglioma).

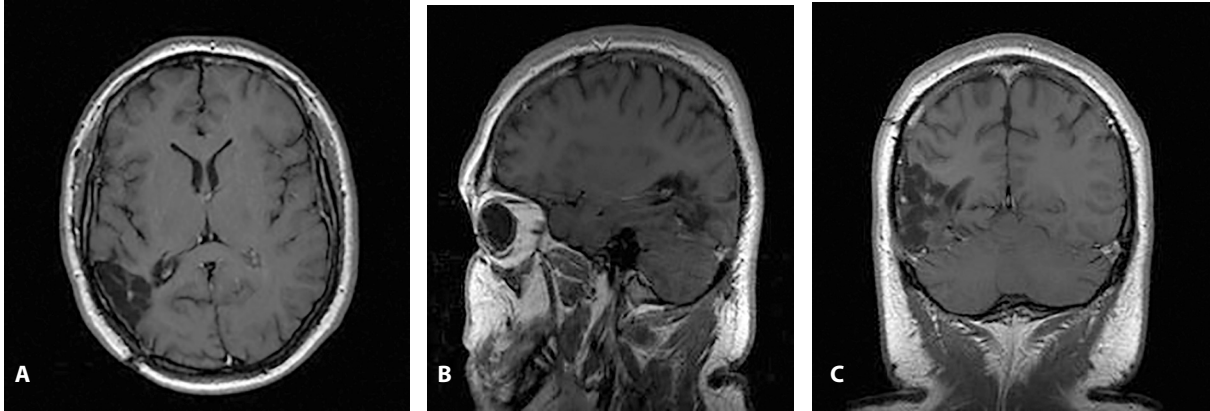


Figure 4. Postoperative axial (A), sagittal (B), and coronal (C) MRI.

Discussion

We analyzed 27 consecutive patients who were operated on for pediatric brain tumor. Patients were admitted at a children's hospital for symptoms of high intracranial pressure, seizure, or neurological deficit. After radiological diagnosis and preoperative preparation, patients were transferred to the department of neurosurgery for tumor resection. In 2 cases, an emergency surgery was done for a ventriculoperitoneal shunt as a first treatment step. The most common form of treatment was surgical removal. Follow-up and additional treatment with irradiation and chemotherapy depended on the result of histopathology. All our cases presented as single grade tumors. Some brain neoplasms only manifested as a single grade — for example, pilocytic astrocytoma, subependymoma, subependymal giant cell astrocytoma, myxopapillary ependymoma, and most glioneuronal tumors (5). In our study, the tumors manifested as a single grade. Among histopathologically benign tumors there was no spontaneous anaplastic transformation.

Regarding embryonal tumors, the categorization of medulloblastomas has undergone extensive changes since publication of the 2007 World Health Organization (WHO) tumor classification. There are now 5 subtypes based on genetic and expression profiles that correspond to histological subtypes only to an extremely limited extent (6). Histological stratification of medulloblastomas based on the 2007 WHO classification has indeed limited prognostic value, although it has long

been recognized that desmoplastic and extensive nodularity variants carry a better prognosis (7), and the large cell anaplastic variants carry a worse prognosis. Also, the degree of anaplasia correlates significantly with clinical outcome (8). Following radiotherapy, chemotherapy, or both, medulloblastomas with extensive nodularity occasionally undergo maturation to tumors dominated by ganglion cells (9).

Three medulloblastoma (11%) were found in our study. Following tumor resection, patients were treated by radiotherapy and chemotherapy. Radiological follow-up implied MRI of the complete neuroaxis.

Diffuse midline glioma was first introduced as diffuse intrinsic pontine glioma (DIPG). Patients are typically young children with brainstem symptoms; signs of CSF obstruction rapidly develops within a few months. On MRI, DIPGs often present as a large pontine mass, which may encase the basilar artery (10). Contrast enhancement is usually focal. Infiltration of neighboring structures has frequently been observed. These tumors are diverse histopathologically, although they commonly show a uniform population of cells that resemble neoplastic astrocytes. Necrosis and vascular proliferation are also seen in some cases (11). Extrapontine lesions typically affect older children and occasionally adults. Since most cases contain the typical mutational profile, the term proposed by the WHO Working Group is a diffuse midline glioma H3 K27M-mutant (3).

Among the astrocytomas in our study, the most frequent tumor was pilocytic astrocytoma (34%) and then Grade II astrocytoma (7%). The astrocytomas were located in cerebellar hemispheres and they were completely removed during surgery. There was no tumor remnant found during the follow-up period. One-third of pediatric brain tumors in our study were pilocytic astrocytomas. These tumors were often cystic with a solid part, and they tended to be well-circumscribed. Tumor location could prohibit access to the neoplasm and lead to an incomplete resection. Removal of the tumor will generally allow functional survival for many years (12).

Craniopharyngiomas are histologically benign neuroepithelial tumors of the central nervous system (CNS) with malignant behavior, which are predominantly observed in children aged 5 to 10 years. These lesions tend to invade surrounding structures and to recur after a total resection (13, 14). Two of 4 craniopharyngiomas in this study showed a recurrence during the follow-up period, and reoperation was needed.

Ganglioglioma is a common seizure-associated tumor, and surgery is currently considered the treatment of choice. During the follow-up period, all 4 ganglioma patients in this study became seizure-free. These data indicated that surgical treatment might result in excellent seizure control for patients with ganglioglioma (15). Genetically based classifications are a great step forward and a valuable basis for future clinical trials. From a clinical point of view, the relevance of tumor grades may not be as significant as before.

Pediatric brain tumor symptoms vary according to the size, type, and location of the tumor. In our study the most frequent symptoms were headache and vomiting. Symptoms may occur when a tumor presses on a nerve or damages certain parts of the brain. They may also occur when the brain swells or there is fluid build-up in the skull. The most common symptoms include the following: headaches (usually worse in the morning); nausea or vomiting; changes in speech, vision, or hearing; problems balancing or walking; changes in mood, personality or ability to concentrate; problems

with memory; muscle jerking or twitching (seizures or convulsions); and numbness or tingling in the arms or legs.

Brain tumors presenting during the first year of life is a different subset of tumors than those presenting later in childhood. In a busy neurosurgical unit in a children's hospital, they represented approximately 8% of the children admitted with brain tumors, an average of only ~3 admissions per year (16). Ninety percent of brain tumors in neonates are of neuroectodermal origin, teratoma being the most common. Other supratentorial tumors include astrocytoma, choroid plexus tumors, ependymomas, and craniopharyngiomas. Some of these tumors may be congenital (17).

The youngest patient in this study was 6-months-old and treated surgically for a large compressive ganglioglioma of the left-brain hemisphere. Postoperative functional and psychophysical development in this patient proceeded normally without neurological deficit. There was 1 patient with a large compressive choroid plexus carcinoma (CPC) who was treated first via tumor resection, followed by radiotherapy and chemotherapy. CPCs are rare neoplasms of neuroectodermal origin that correspond to WHO Grade III tumors. Due to their rarity, reports on CPCs most often focus on single cases or single-institution experiences with a limited number of patients

Many posterior fossa tumors escape diagnosis until they are large in size due to the elasticity of the infant skull, which is proof of the adaptability of the developing nervous system to compensate for deficits, and of the difficulty in examining a patient with a limited neurologic repertoire and an inability to cooperate. The most common presenting manifestations are vomiting, arrest or regression of psychomotor development, macrocrania, and poor feeding or failure to thrive. They may also present with seizures as one of significant long-term sequelae that influences treatment-related morbidity (18).

A small sample size in this study is a limitation in statistical power and conclusions. We presented our experience in study of 27 consecutive patients who were admitted to department of neurosurgery

for a surgical treatment. We did not include patients who are not treated surgically for extensive infiltrative brain tumors and infiltrative brain stem tumors with poor general and neurological status. These patients have been treated and followed up by pediatrics, neuro-oncologists, and radiation oncologists.

We decided to present the surgical results of 2 cases: one of the most common (pilocytic astrocytoma — WHO Grade I) and one of the rarest (choroid plexus carcinoma — WHO Grade III) pediatric brain tumors with a different supratentorial and infratentorial localization and a different further prognosis. The tumors were removed completely with a good postoperative radiological result on MRI. Further radiological follow-up showed good results in patients with astrocytoma and a recurrence in patients with choroid plexus carcinoma.

Conclusion

Pediatric brain tumors are the most common solid tumors in children and the leading cause of cancer-related morbidity and mortality. Over the past decades, considerable advances have been made in neurosurgery, radiotherapy, and chemotherapy that result in improved survival and cure rates for children with brain tumors. Prompt medical attention and aggressive therapy are important for the best prognosis.

What Is Already Known on this Topic:

Prognosis and long-term survival of pediatric brain tumors are based upon the type of tumor, tumor location and grade, the length of time the child has exhibited symptoms, the speed of growth, and treatment options. While survival and cure rates have improved, treatment-related morbidity remains high and significant long-term sequelae are common.

What this Study Adds:

Surgery is a first step in treating brain tumors in children with the goal to remove all or as much of the tumor as possible while maintaining neurological function. A close collaboration between neurosurgery, pediatrics, neuro-oncology, radiation oncology, and diagnostic radiology was essential for a good treatment and prognosis of our patients.

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Conflict of Interest: The authors declare that they have no conflict of interest.

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