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Childhood Brain and Spinal Cord Tumors Treatment Overview (PDQ®)

Health Professional Version

Authors

PDQ Pediatric Treatment Editorial Board.

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This PDQ cancer information summary for health professionals provides comprehensive, peer-reviewed, evidence-based information about the treatment of childhood brain and spinal cord tumors. It is intended as a resource to inform and assist clinicians who care for cancer patients. It does not provide formal guidelines or recommendations for making health care decisions.

This summary is reviewed regularly and updated as necessary by the PDQ Pediatric Treatment Editorial Board, which is editorially independent of the National Cancer Institute (NCI). The summary reflects an independent review of the literature and does not represent a policy statement of NCI or the National Institutes of Health (NIH).

General Information About Childhood Brain and Spinal Cord Tumors

Dramatic improvements in survival have been achieved for children and adolescents with cancer. Between 1975 and 2010, childhood cancer mortality decreased by more than 50%.[1] Childhood and adolescent cancer survivors require close monitoring because cancer therapy side effects may persist or develop months or years after treatment. Refer to the PDQ summary on Late Effects of Treatment for Childhood Cancer for specific information about the incidence, type, and monitoring of late effects in childhood and adolescent cancer survivors.

Primary brain tumors are a diverse group of diseases that together constitute the most common solid tumor of childhood. Brain tumors are classified by histology, but tumor location and extent of spread are also important factors that affect treatment and prognosis. Immunohistochemical analysis, cytogenetic and molecular genetic findings, and measures of proliferative activity are increasingly used in tumor diagnosis and classification.[2]

Incidence

The Central Brain Tumor Registry of the United States (CBTRUS) estimates that approximately 4,300 U.S. children are diagnosed each year.[3]

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Classification of Central Nervous System Tumors

The classification of childhood central nervous system (CNS) tumors is based on histology and location.[1] Tumors are classically categorized as infratentorial, supratentorial, parasellar, or spinal. Immunohistochemical analysis,

cytogenetic and molecular genetic findings, and measures of proliferative activity are increasingly used in tumor diagnosis and classification.

Primary CNS spinal cord tumors comprise approximately 1% to 2% of all childhood CNS tumors. The classification of spinal cord tumors is based on histopathologic characteristics of the tumor and does not differ from that of primary brain tumors.[1]

Infratentorial (posterior fossa) tumors include the following:

1. Cerebellar astrocytomas (most commonly pilocytic, but also diffuse and, less frequently, anaplastic astrocytoma or glioblastoma).
2. Medulloblastomas (including classic, desmoplastic/nodular, extensive nodularity, anaplastic, or large cell variants).
3. Ependymomas (papillary, clear cell, tanycytic, or anaplastic).
4. Brain stem gliomas (typically diffuse midline glioma, H3 K27M-mutant, and other diffuse midline gliomas; focal, tectal, and exophytic cervicomedullary gliomas are most frequently pilocytic astrocytomas).
5. Atypical teratoid/rhabdoid tumors.
6. Choroid plexus tumors (papillomas and carcinomas).

Supratentorial tumors include the following:

1. Low-grade cerebral hemispheric astrocytomas (grade I [pilocytic] astrocytomas or grade II [diffuse] astrocytomas).
2. High-grade or malignant astrocytomas (anaplastic astrocytomas and glioblastoma).
3. Oligodendrogliomas (low-grade, anaplastic, and mixed oligoastrocytomas).
4. Neuronal and mixed neuronal glial tumors (13 variants, including gangliogliomas, desmoplastic infantile astrocytoma/gangliogliomas, dysembryoplastic neuroepithelial tumors, and papillary glioneuronal tumors).
5. Other low-grade gliomas (including subependymal giant cell tumors and pleomorphic xanthoastrocytoma).
6. Embryonal tumors, including embryonal tumor with multilayered rosettes (ETMR) (*C19MC*-altered or not otherwise specified), medulloepithelioma, CNS neuroblastoma, CNS ganglioneuroblastoma, CNS embryonal tumor, and CNS embryonal tumor with rhabdoid features.
7. Atypical teratoid/rhabdoid tumors.
8. Ependymomas (papillary, clear cell, tanycytic, *RELA*–fusion positive, or anaplastic).
9. Meningiomas (grades I, II, and III).
10. Choroid plexus tumors (papillomas, carcinomas, and atypical choroid plexus tumor).
11. Tumors of the pineal region (pineocytomas, pineoblastomas, pineal parenchymal tumors of intermediate differentiation, and papillary tumors of the pineal region) and germ cell tumors.
12. Metastasis (rare) from extraneural malignancies.

Parasellar tumors include the following:

1. Craniopharyngiomas.

2. Diencephalic astrocytomas (central tumors involving the chiasm, hypothalamus, and/or thalamus) that are generally low-grade (including astrocytomas, grade I [pilocytic] or grade II [diffuse]).
3. Germ cell tumors (germinomas or nongerminomatous).
4. Rarely, embryonal and glial tumors.

Spinal cord tumors include the following:

1. Low-grade astrocytomas (grade I [pilocytic] astrocytomas or grade II [diffuse] astrocytomas).
2. High-grade or malignant astrocytomas (anaplastic astrocytomas and glioblastoma [grade III or grade IV]).
3. Gangliogliomas.
4. Ependymomas (often myxopapillary).
5. Meningiomas.

References

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General Approach to Care for Children With Brain and Spinal Cord Tumors

Important concepts that should be understood by those treating and caring for a child who has a brain tumor or spinal cord tumor include the following:

1. The cause of most childhood brain tumors remains unknown; however, germline mutations are becoming increasingly recognized as cancer-predisposing, as they are identified in up to 8% of children with cancer.[1,2]
2. Selection of an appropriate therapy can only occur if the correct diagnosis is made and the stage of the disease is accurately determined.
3. Children with primary brain or spinal cord tumors represent a major therapy challenge that, for optimal results, requires the coordinated efforts of pediatric specialists in fields such as neurosurgery, neuropathology, radiation oncology, pediatric oncology, neuro-oncology, neurology, rehabilitation, neuroradiology, endocrinology, and psychology, who have special expertise in the care of patients with these diseases.[3,4] For example, radiation therapy of pediatric brain tumors is technically demanding and should be performed in centers that have experience in this area.
4. For most childhood brain and spinal cord tumors, the optimal treatment regimen has not been determined. Children who have brain and spinal cord tumors should be considered for enrollment in a clinical trial when an appropriate study is available. Such clinical trials are carried out by institutions and cooperative groups. Survival of childhood cancer has increased as a result of clinical trials that have attempted to improve upon the best accepted therapy available. Clinical trials in pediatrics are designed to compare new therapy with treatment that is currently accepted as standard. This comparison may be done in a randomized study of two treatment arms or by evaluating a single new treatment and then comparing the results with those previously obtained from existing therapy. Information about ongoing clinical trials is available from the NCI website.
5. While more than 70% of children diagnosed with brain tumors will survive for more than 5 years after diagnosis, survival rates are wide-ranging depending on tumor type and stage. Long-term sequelae related both to the effects of the tumor and its treatment are common.[5-7] Debilitating effects on growth and neurologic development have frequently been observed after radiation therapy, especially in younger children. Secondary

tumors have increasingly been diagnosed in long-term survivors.[8] The dose and volume of radiation therapy appropriate for specific tumor types continues to be refined, and techniques for its administration (e.g., more conformal targeted-field design and protons) have evolved to mitigate the potential for adverse effects. In addition, the role of chemotherapy in allowing a delay or reduction in the administration of radiation therapy is under study, and preliminary results suggest that chemotherapy can be used to delay, limit, and sometimes obviate, the need for radiation therapy in children with benign and malignant lesions.[9-11] Long-term management of these patients is complex and requires a multidisciplinary approach.

(Refer to the PDQ summary on Late Effects of Treatment for Childhood Cancer for more information about possible long-term or late effects.)

6. Guidelines for pediatric cancer centers and their role in the treatment of pediatric patients with cancer have been outlined by the American Academy of Pediatrics.[12]

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Treatment of Newly Diagnosed and Recurrent Childhood Brain Tumors

Presently, there is no uniformly accepted staging system for most childhood brain tumors. These tumors are classified and treated on the basis of their histology and location within the brain (refer to the Table below). With advances in molecular data, it is conceivable that genomic factors will refine classification approaches and will be increasingly used to stratify patients entered on clinical trials.

Newly Diagnosed or Recurrent Tumor Type and Its Related PDQ Treatment Summary

Tumor Type	Pathologic Subtype	Related PDQ Treatment Summary
Astrocytomas and Other Tumors of Glial Origin		
– *Low-Grade Astrocytomas*	Diffuse astrocytoma, *IDH*-mutant, *IDH*-wild type, or NOS	Childhood Astrocytomas Treatment
	Pilocytic astrocytoma	
	Pleomorphic xanthoastrocytoma	
	Subependymal giant cell astrocytoma	
– *High-Grade Astrocytomas*	Anaplastic astrocytoma, *IDH*-mutant or *IDH*-wild type	Childhood Astrocytomas Treatment
	Anaplastic pleomorphic xanthoastrocytoma	
	Diffuse midline glioma, H3 K27M-mutant	
	Glioblastoma, *IDH*-mutant	
	Glioblastoma, *IDH*-wildtype	
– *Other Astrocytomas or Gliomas*	Angiocentric glioma	Childhood Astrocytomas Treatment
	Astroblastoma[a]	
	Choroid glioma of the third ventricle	
	Pilomyxoid astrocytoma[a]	
Brain Stem Glioma		
	Diffuse intrinsic pontine glioma, H3 K27M-mutant	Childhood Brain Stem Glioma Treatment
	Focal or low-grade brain stem glioma	
CNS Embryonal Tumors		
– *Medulloblastomas*	Medulloblastoma, WNT-activated	Childhood Medulloblastoma and Other CNS Embryonal Tumors Treatment
	Medulloblastoma, SHH-activated and *TP53*-mutant	
	Medulloblastoma, SHH-activated and *TP53*-wildtype	
	Medulloblastoma, non-WNT/non-SHH	
– *Nonmedulloblastomas*	CNS ganglioneuroblastoma	
	CNS neuroblastoma	
	Embryonal tumor with multilayered rosettes, *C19MC*-altered or NOS	
	Medulloepithelioma	

Tumor Type	Pathologic Subtype	Related PDQ Treatment Summary
– *CNS Atypical Teratoid/Rhabdoid Tumor*		Childhood CNS Atypical Teratoid/Rhabdoid Tumor Treatment
Pineal Parenchymal Tumors	Pineoblastoma	Childhood Medulloblastoma and Other CNS Embryonal Tumors Treatment
CNS Germ Cell Tumors		
– *Germinomas*		Childhood CNS Germ Cell Tumors Treatment
– *Teratomas*	Immature teratoma	
	Mature teratoma	
	Teratoma with malignant transformation	
– *Nongerminomatous Germ Cell Tumors*	Choriocarcinoma	
	Embryonal carcinoma	
	Mixed germ cell tumor	
	Yolk sac tumor	
Craniopharyngioma		Childhood Craniopharyngioma Treatment
Ependymoma		
	Subependymoma (WHO grade I)	Childhood Ependymoma Treatment
	Myxopapillary ependymoma (WHO grade I)	
	Ependymoma (WHO grade II)	
	Ependymoma, *RELA* fusion–positive (WHO grade II or grade III)	
	Anaplastic ependymoma (WHO grade III)	

CNS = central nervous system; NOS = not otherwise specified; WHO = World Health Organization.
[a]Grade uncertain.

Relapse is not uncommon in both low-grade and malignant childhood brain tumors and may occur many years after initial treatment. Disease may occur at the primary tumor site or, especially in malignant tumors, at noncontiguous central nervous system (CNS) sites. Systemic relapse is rare but may occur in some tumor types. At recurrence, a complete evaluation for extent of relapse is indicated for all malignant tumors and, at times, for lower-grade lesions. Biopsy or surgical re-resection may be necessary for confirmation of relapse or the diagnosis of tumor transformation, which can include a change in grade and molecular makeup.[1,2] Other entities, such as secondary tumor and treatment-related intratumoral necrosis or frank brain necrosis, may be clinically indistinguishable from tumor recurrence.[3] The determination of the need for surgical intervention must be individualized on the basis of the initial tumor type, the length of time between initial treatment and the reappearance of the lesion, and other clinical parameters.

Early-phase therapeutic trials may be available for selected patients via Children's Oncology Group phase I institutions, the Pediatric Brain Tumor Consortium, or other entities.

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Treatment of Newly Diagnosed and Recurrent Childhood Spinal Cord Tumors

There is no uniformly accepted staging system for childhood primary spinal cord tumors. These tumors are classified and treated based on their location within the spinal cord, tumor extent at diagnosis, and histology. Refer to the following PDQ summaries for more information on the staging and treatment of newly diagnosed and recurrent childhood spinal cord tumors:

- Childhood Astrocytomas Treatment.
- Childhood Medulloblastoma and Other Central Nervous System Embryonal Tumors Treatment.
- Childhood Ependymoma Treatment.

Changes to This Summary (03/17/2020)

The PDQ cancer information summaries are reviewed regularly and updated as new information becomes available. This section describes the latest changes made to this summary as of the date above.

This summary was comprehensively reviewed.

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Purpose of This Summary

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