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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

Primary brain tumors are a diverse group of diseases that together constitute the most common solid tumor of childhood. The Central Brain Tumor Registry of the United States (CBTRUS) estimates that approximately 4,300 U.S. children are diagnosed each year.[1]

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]

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%.[3] 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.

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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 therapies with treatments that are 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 using 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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Staging, Classification, and Treatment of Newly Diagnosed and Recurrent Childhood Brain and Spinal Cord Tumors

Presently, there is no uniformly accepted staging system for most childhood brain tumors.

The classification of childhood central nervous system (CNS) tumors is based on histology, location, and extent of spread (refer to the Table below).[1] Immunohistochemical analysis, cytogenetic and molecular genetic findings, and measures of proliferative activity are increasingly used in tumor diagnosis and classification.[1] 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.

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]

CNS Tumor Type, Pathologic Subtype, and Its Related PDQ Treatment Summary

Tumor Type (Based on the 2016 WHO Classification)	Pathologic Subtype (Based on the 2016 WHO Classification)	Related PDQ Treatment Summary
Diffuse astrocytic tumors	Diffuse astrocytoma, *IDH*-mutant and *IDH*-wildtype	Childhood Astrocytomas Treatment
	Anaplastic astrocytoma, *IDH*-mutant and *IDH*-wildtype	
	Glioblastoma, *IDH*-mutant and *IDH*-wildtype	
	Diffuse midline glioma, H3K27M-mutant	Childhood Astrocytomas Treatment
		Childhood Brain Stem Glioma Treatment
Other astrocytic tumors	Pilocytic astrocytoma	Childhood Astrocytomas Treatment
		Childhood Brain Stem Glioma Treatment
	Subependymal giant cell astrocytoma	Childhood Astrocytomas Treatment
	Pleomorphic xanthoastrocytoma	
	Anaplastic pleomorphic xanthoastrocytoma	
Ependymal tumors	Subependymoma	Childhood Ependymoma Treatment
	Myxopapillary ependymoma	
	Ependymoma	
	Ependymoma, *RELA* fusion–positive	
	Anaplastic ependymoma	
Other gliomas	Angiocentric glioma	Childhood Astrocytomas Treatment
	Astroblastoma	
Neuronal and mixed neuronal-glial tumors	Dysembryoplastic neuroepithelial tumor	Childhood Astrocytomas Treatment
	Ganglioglioma	
	Desmoplastic infantile astrocytoma and ganglioglioma	

Tumor Type (Based on the 2016 WHO Classification)	Pathologic Subtype (Based on the 2016 WHO Classification)	Related PDQ Treatment Summary
	Papillary glioneuronal tumor	
	Rosette-forming glioneuronal tumor	
	Diffuse leptomeningeal glioneuronal tumor	
	Extraventricular neurocytoma	
	Cerebellar liponeurocytoma	
	Paraganglioma	
Tumors of the pineal region	Pineoblastoma	Childhood Medulloblastoma and Other Central Nervous System Embryonal Tumors Treatment
Embryonal tumors	Medulloblastoma, *WNT*-activated	Childhood Medulloblastoma and Other Central Nervous System Embryonal Tumors Treatment
	Medulloblastoma, SHH-activated and *TP53*-mutant; Medulloblastoma, SHH-activated and *TP53*-wildtype	
	Medulloblastoma, non-*WNT*/non-SHH group 3	
	Medulloblastoma, non-*WNT*/non-SHH group 4	
	Medulloblastoma, classic	
	Medulloblastoma, desmoplastic/nodular	
	Medulloblastoma with extensive nodularity	
	Medulloblastoma, large cell/anaplastic	
	Embryonal tumor with multilayered rosettes, *C19MC*-altered	
	Medulloepithelioma	
	CNS neuroblastoma	
	CNS ganglioneuroblastoma	
	Atypical teratoid/rhabdoid tumor	Childhood Central Nervous System Atypical Teratoid/Rhabdoid Tumor Treatment
	CNS embryonal tumor with rhabdoid features	Childhood Medulloblastoma and Other Central Nervous System Embryonal Tumors Treatment
Germ cell tumors	Germinoma	Childhood Central Nervous System Germ Cell Tumors Treatment
	Embryonal carcinoma	
	Yolk sac tumor	
	Choriocarcinoma	
	Mature teratoma	
	Immature teratoma	
	Teratoma with malignant transformation	
	Mixed germ cell tumor	

Tumor Type (Based on the 2016 WHO Classification)	Pathologic Subtype (Based on the 2016 WHO Classification)	Related PDQ Treatment Summary
Tumors of the sellar region	Adamantinomatous craniopharyngioma	Childhood Craniopharyngioma Treatment
	Papillary craniopharyngioma	

CNS = central nervous system; WHO = World Health Organization.

Relapse is not uncommon in both low-grade and malignant childhood brain tumors and may occur many years after initial treatment. Disease relapse may occur at the primary tumor site or, especially in malignant tumors, at noncontiguous 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.[2,3] Other entities, such as secondary tumor and treatment-related intratumoral necrosis or frank brain necrosis, may be clinically indistinguishable from tumor recurrence.[4] Determining 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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Changes to This Summary (10/09/2020)

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.

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Purpose of This Summary

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