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Childhood Craniopharyngioma Treatment (PDQ®)

Health Professional Version

Authors

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This PDQ cancer information summary for health professionals provides comprehensive, peer-reviewed, evidence-based information about the treatment of childhood craniopharyngioma. 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 Craniopharyngioma

Primary brain tumors, including craniopharyngiomas, are a diverse group of diseases that together constitute the most common solid tumor of childhood. Brain tumors are classified according to histology, but tumor location and extent of spread are important factors that affect treatment and prognosis.

Craniopharyngiomas are uncommon pediatric brain tumors. They are believed to be congenital in origin, arising from ectodermal remnants, Rathke cleft, or other embryonal epithelium, and often occur in the suprasellar region with an intrasellar portion. Magnetic resonance imaging (MRI) and computed tomography (CT) imaging are used to diagnose craniopharyngiomas, but histologic confirmation is generally required before treatment. The treatment of patients with newly diagnosed craniopharyngiomas may include a combination of surgery, radiation therapy, cyst drainage, and/or intracystic interferon-alpha. The treatment of patients with recurrent craniopharyngiomas depends on the initial treatment used. Regardless of treatment given, the 5-year and 10-year survival rates exceed 90% for children between the ages of 0 and 14 years.[1]

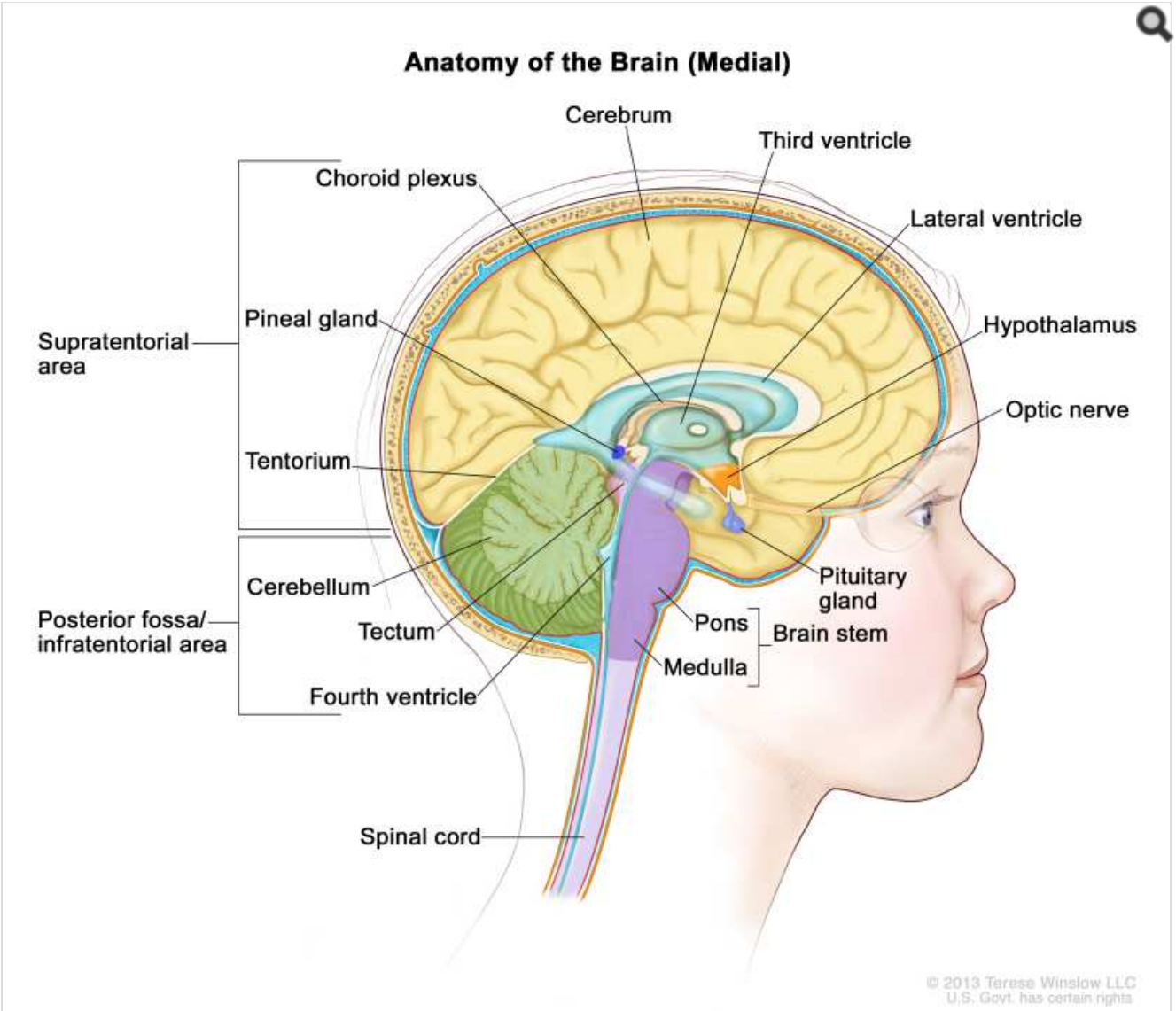
The PDQ childhood brain tumor treatment summaries are organized primarily according to the World Health Organization classification of nervous system tumors.[2] For a full description of the classification of nervous system tumors and a link to the corresponding treatment summary for each type of brain tumor, refer to the PDQ summary on Childhood Brain and Spinal Cord Tumors Treatment Overview.

Incidence

Craniopharyngiomas are relatively uncommon, accounting for about 6% of all intracranial tumors in children.[3,4]

No predisposing factors have been identified.

Anatomy



Anatomy of the inside of the brain, showing the pineal and pituitary glands, optic nerve, ventricles (with cerebrospinal fluid shown in blue), and other parts of the brain. The tentorium separates the cerebrum from the cerebellum. The infratentorium (posterior fossa) is the region below the tentorium that contains the brain stem, cerebellum, and fourth ventricle. The supratentorium is the region above the tentorium and denotes the region that contains the cerebrum.

Clinical Presentation

Craniopharyngiomas occur in the region of the pituitary gland, and endocrine function may be affected. Additionally, their closeness to the optic nerves and chiasm may result in vision problems. Some patients present with obstructive hydrocephalus caused by tumor growth within the third ventricle. Rarely, tumors may extend into the posterior fossa, and patients may present with headache, diplopia, ataxia, and hearing loss.[5]

Diagnostic Evaluation

CT scans and MRI scans are often diagnostic for childhood craniopharyngiomas, with most tumors demonstrating intratumoral calcifications and a solid and cystic component. MRI of the spinal axis is not routinely performed.

Craniopharyngiomas without calcification may be confused with other tumor types, including germ cell tumors, hypothalamic/chiasmatic astrocytomas, or Langerhans cell histiocytosis. Biopsy or resection is required to confirm the diagnosis.[6]

Apart from imaging, patients often undergo endocrine testing and formal vision examination, including visual-field evaluation.

Prognosis

Regardless of the treatment modality, the long-term event-free survival rate is approximately 65% in children,[3,4] with 5-year and 10-year overall survival rates higher than 90% in children between the ages of 0 and 14 years.[1,7-9]

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Histopathologic Classification of Childhood Craniopharyngioma

Craniopharyngiomas are histologically benign and often occur in the suprasellar region, with an intrasellar portion. They may be locally invasive and typically do not metastasize to remote brain locations.

Craniopharyngiomas are classified as one of the following:

- **Adamantinomatous:** Adamantinomatous craniopharyngioma is the type found most frequently in children.[1] These tumors are typically composed of a solid portion formed by nests and trabeculae of epithelial tumor cells, with an abundance of calcification, and a cystic component that is filled with a dark, oily fluid. Wet keratin is also characteristic. Adamantinomatous craniopharyngiomas are more locally aggressive than are papillary tumors and have a significantly higher rate of recurrence.[2] Activating *CTNNB1* gene mutations are found in most adamantinomatous tumors.[3-5]
- **Papillary:** Papillary craniopharyngiomas occur primarily in adults. *BRAF* V600E mutations are observed in nearly all papillary craniopharyngiomas.[4,5]

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Stage Information for Childhood Craniopharyngioma

There is no generally applied staging system for childhood craniopharyngiomas. For treatment purposes, patients are grouped as having newly diagnosed or recurrent disease.

Treatment Option Overview for Childhood Craniopharyngioma

Table 1 describes the treatment options for newly diagnosed and recurrent childhood craniopharyngioma.

Table 1. Treatment Options for Childhood Craniopharyngioma

Treatment Group	Treatment Options
Newly diagnosed childhood craniopharyngioma	Complete resection with or without radiation therapy
	Subtotal resection with radiation therapy
	Primary cyst drainage with or without radiation therapy
	Intracystic therapy (i.e., interferon-alpha)
Recurrent childhood craniopharyngioma	Surgery
	Radiation therapy, including radiosurgery
	Intracavitary instillation of radioactive phosphorus P 32, bleomycin, or interferon-alpha, for those with cystic recurrences
	Systemic peginterferon alpha-2b

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.)

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Newly Diagnosed Childhood Craniopharyngioma Treatment

Treatment Options for Newly Diagnosed Childhood Craniopharyngioma

There is no consensus on the optimal treatment for patients with newly diagnosed craniopharyngioma, in part because of the lack of prospective randomized trials that compare the different treatment options. Treatment is individualized on the basis of factors that include the following:

- Tumor size.
- Tumor location.
- Extension of the tumor.
- Potential short-term and long-term toxicity.

Treatment options for newly diagnosed childhood craniopharyngioma include the following:

1. Complete resection with or without radiation therapy.
2. Subtotal resection with radiation therapy.

3. Primary cyst drainage with or without radiation therapy.
4. Intracystic therapy (i.e., interferon-alpha).

Complete resection with or without radiation therapy

It may be possible to remove all visible tumor and achieve long-term disease control.[1][Level of evidence: 3iA]; [2][Level of evidence: 3iiiB]; [3][Level of evidence: 3iiiC] A 5-year progression-free survival (PFS) rate of about 65% has been reported.[4] Gross-total resection is often technically challenging because the tumor is surrounded by vital structures, including the optic nerves and chiasm, the carotid artery and its branches, the hypothalamus, and the third cranial nerve. These structures may limit the ability to remove the entire tumor.

Many surgical approaches have been described, and the choice is determined by tumor size, location, and extension. Surgical approaches include the following:

- **Craniotomy:** As noted above, gross-total resection may be technically challenging because the tumor is surrounded by vital structures. The surgeon often has a limited view of the hypothalamic and sellar regions, and portions of the mass may remain after surgery, accounting for some recurrences. An understanding of the complex variations in how the tumors grow anatomically may help facilitate gross-total resection.[5] Nonetheless, almost all craniopharyngiomas have an attachment to the pituitary stalk, and of the patients who undergo complete resection, virtually all will require lifelong pituitary hormone replacement with multiple medications.[2,6]

  Complications of complete resection include the following:

  - Obesity, which can be life-threatening.[7]
  - Need for hormone replacement therapy.[8]
  - Severe behavioral problems.[8]
  - Blindness.
  - Seizures.
  - Spinal fluid leak.
  - False aneurysms.
  - Difficulty with eye movements.
  - Death from intraoperative hemorrhage, hypothalamic damage, or stroke (rare).

- **Transsphenoidal approach:** A transsphenoidal approach may be possible for some small tumors located entirely within the sella.[9][Level of evidence: 3iiiC] The development of expanded endonasal techniques with endoscopic visualization have allowed increased use of this approach, even for sizeable childhood tumors, which is similar to the experience in adults.[10] A complete resection can be obtained using this approach, with associated complications of panhypopituitarism and the risk of cerebrospinal fluid leaks.[11] When an endonasal approach is not possible, a craniotomy is required.

If the surgeon indicates that the tumor was not completely removed or if postoperative imaging reveals residual craniopharyngioma, radiation therapy may be recommended to prevent early progression (refer to the Subtotal resection with radiation therapy section of this summary for more information).[12][Level of evidence: 3iiiDiii]

Periodic surveillance using magnetic resonance imaging is performed for several years after complete resection because of the possibility of tumor recurrence.

Subtotal resection with radiation therapy

The goal of limited surgery is to establish a diagnosis, drain any cysts, and decompress the optic nerves. No attempt is made to remove tumor from the pituitary stalk or hypothalamus in an effort to minimize the late effects associated with complete resection.[13]

The surgical procedure is often followed by radiation therapy, with a 5-year PFS rate of about 70% to 90% [4,14]; [15][Level of evidence: 3iDiii] and 10-year overall survival rates exceeding 90%.[16][Level of evidence: 3iiA]; [17][Level of evidence: 3iiiDiii] The standard approach to radiation therapy involves fractionated external-beam radiation, with a recommended dose of 50 Gy to 54 Gy, in 1.8-Gy fractions, restricting the optic chiasm dose to 54 Gy.[18-21] Transient cyst enlargement may be noted soon after radiation therapy but generally resolves without further intervention.[22][Level of evidence: 3iDiv]

A systematic review of 109 reports that described extent of resection found that subtotal resection plus radiation therapy was associated with rates of tumor control similar to those for gross-total resection. It was also reported that both approaches were associated with PFS rates higher than those for subtotal resection alone.[17][Level of evidence: 3iiiDiii]

Surgical complications with a subtotal resection are less likely than with complete resection. Complications of radiation therapy include the following:

- Loss of pituitary hormonal function.
- Cognitive dysfunction.
- Development of late strokes and vascular malformations.
- Delayed blindness.
- Development of second tumors.
- Malignant transformation of the primary tumor within the radiation field (rare).[23,24]

Newer radiation technologies such as intensity-modulated photon therapy and proton therapy may reduce the radiation dose to uninvolved parts of the brain and spare normal tissue. When these highly conformal radiation treatments are employed, interim imaging is commonly performed to detect changes in cyst volume, with treatment plans modified as appropriate.[21,25,26] It is unknown whether such technologies reduce late effects from radiation.[15,21,26,27]

Tumor progression remains a concern, and it is usually not possible to repeat a full course of standard fractionated radiation. In selected cases, stereotactic radiation therapy can be delivered as a single large dose of radiation to a small field.[28][Level of evidence: 3iC] Proximity of the craniopharyngioma to vital structures, particularly the optic nerves, limits this to small tumors within the sella.[29][Level of evidence: 3iiiDiii]

Primary cyst drainage with or without radiation therapy

For predominantly cystic craniopharyngiomas, stereotactic drainage of the cyst followed by radiation therapy may be a viable alternative treatment to attempted surgical resection. This procedure may also allow the surgeon to use a two-stage approach: first draining the cyst via the implanted catheter, to relieve pressure and complicating symptoms; and then later resecting the tumor or employing radiation therapy.[30]

Intracystic therapy

Intracystic interferon-alpha may also be a treatment option for primary cystic lesions, after ensuring the integrity of the cyst wall, to delay the need for alternative therapies.[31]

Current Clinical Trials

Use our advanced clinical trial search to find NCI-supported cancer clinical trials that are now enrolling patients. The search can be narrowed by location of the trial, type of treatment, name of the drug, and other criteria. General information about clinical trials is also available.

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Recurrent Childhood Craniopharyngioma Treatment

Treatment Options for Recurrent Childhood Craniopharyngioma

Recurrence of craniopharyngioma occurs in approximately 35% of patients regardless of primary therapy.[1]

Treatment options for recurrent childhood craniopharyngioma include the following:

1. Surgery.
2. Radiation therapy, including radiosurgery.
3. Intracavitary instillation of radioactive phosphorus P 32 (32P), bleomycin, or interferon-alpha, for those with cystic recurrences.
4. Systemic peginterferon alpha-2b.

The management of recurrent craniopharyngioma is determined largely by previous therapy. Repeat attempts at gross-total resections are difficult, and long-term disease control is achieved less often.[2][Level of evidence: 3iiiDi] Complications are more frequent than with initial surgery.[3][Level of evidence: 3iiiDi] If not previously employed, external-beam radiation therapy is an option, including consideration of radiosurgery in selected circumstances.[4][Level of evidence: 3iiiDiii]

Cystic recurrences may be treated with intracavitary instillation of varying agents via placement of an Ommaya catheter.[5] These agents have included radioactive 32P or other radioactive compounds,[6-8]; [9][Level of evidence: 2A] bleomycin,[10]; [11][Level of evidence: 3iiiDiii] or interferon-alpha.[12]; [13][Level of evidence: 3iiiB]; [14][Level of evidence: 3iiiDi] These strategies have been found to be useful in certain cases, and a low risk of complications has been reported. However, none of these approaches have shown efficacy against solid portions of the tumor.

Although systemic therapy is generally not utilized, a small series has shown that the use of subcutaneous peginterferon alpha-2b to manage cystic recurrences can result in durable responses.[15][Level of evidence: 3iiiDiii] In addition, case reports demonstrating dramatic tumor response to BRAF inhibitors in adults with papillary craniopharyngiomas suggest that there may be a role for BRAF inhibitor therapy in the rare setting of a child with a papillary craniopharyngioma.[16,17]

Treatment Options Under Clinical Evaluation for Recurrent Childhood Craniopharyngioma

Early-phase therapeutic trials may be available for selected patients. These trials may be available via the Children's Oncology Group (COG), the Pediatric Brain Tumor Consortium, or other entities. Information about National Cancer

Institute (NCI)–supported clinical trials can be found on the NCI website. For information about clinical trials sponsored by other organizations, refer to the ClinicalTrials.gov website.

The following is an example of a national and/or institutional clinical trial that is currently being conducted:

- **APEC1621 (NCT03155620)** (Pediatric MATCH: Targeted Therapy Directed by Genetic Testing in Treating Pediatric Patients with Relapsed or Refractory Advanced Solid Tumors, Non-Hodgkin Lymphomas, or Histiocytic Disorders)**:** NCI-COG Pediatric Molecular Analysis for Therapeutic Choice (MATCH), referred to as Pediatric MATCH, will match targeted agents with specific molecular changes identified using a next-generation sequencing targeted assay of more than 4,000 different mutations across more than 160 genes in refractory and recurrent solid tumors. Children and adolescents aged 1 to 21 years are eligible for the trial.

  Tumor tissue from progressive or recurrent disease must be available for molecular characterization. Patients with tumors that have molecular variants addressed by treatment arms included in the trial will be offered treatment on Pediatric MATCH. Additional information can be obtained on the NCI website and ClinicalTrials.gov website.

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Late Effects in Patients Treated for Childhood Craniopharyngioma

Quality-of-life issues are important in this group of patients and are difficult to generalize because of the various treatment modalities. In one series of 261 patients diagnosed with craniopharyngiomas before 2000, hypothalamic involvement was associated with lower overall survival (OS), impaired quality-of-life, and severe obesity.[1][Level of evidence: 3iA]

Late effects of treatment for childhood craniopharyngioma include the following:

- Behavioral issues and memory deficits. Although intelligence quotient is usually maintained, behavioral issues and memory deficits attributed to the frontal lobe and hypothalamus commonly occur.[2,3] Patients with hypothalamic involvement showed impairment in memory and executive functioning.[4]
- Visual disturbances, including visual field and acuity defects.[5][Level of evidence: 3iiiC]
- Endocrine abnormalities. Endocrine abnormalities result in the almost universal need for lifelong endocrine replacement with multiple pituitary hormones.[3]; [6-8][Level of evidence: 3iiiC] A report indicated that adults, despite being treated with long-term growth hormone replacement after childhood-onset craniopharyngioma involving the hypothalamus, were at increased risk of developing cardiovascular disease.[9]
- Decreased height. Growth hormone replacement initiated in childhood results in increases in height without impact on OS and progression-free survival when compared with children who did not receive growth hormone.[10][Level of evidence: 3iiiC] Growth hormone administration beginning 1 year after diagnosis may be associated with early improvements in quality of life when measured at 3 years postdiagnosis.[11][Level of evidence: 3iC]
- Obesity, which can be life-threatening, and the development of metabolic syndrome, including nonalcoholic fatty liver disease.[12,13] Children who undergo complete resection or subtotal resection may develop obesity, suggesting that a predilection to obesity may be a component of the disease itself, as opposed to the result of direct hypothalamic injury.[14][Level of evidence: 3iC]
- Vasculopathies and stroke. Vasculopathies and subsequent strokes may result from local irradiation.[15,16] One cross-sectional cohort study observed a trend suggesting that long-term growth hormone replacement may reduce the risk of stroke.[16]
- Subsequent neoplasms. Subsequent neoplasms may result from local irradiation.[15]

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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Changes to This Summary (11/24/2020)

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.

This summary is written and maintained by the PDQ Pediatric Treatment Editorial Board, which is editorially independent of NCI. The summary reflects an independent review of the literature and does not represent a policy statement of NCI or NIH. More information about summary policies and the role of the PDQ Editorial Boards in maintaining the PDQ summaries can be found on the About This PDQ Summary and PDQ® - NCI's Comprehensive Cancer Database pages.

About This PDQ Summary

Purpose of This Summary

This PDQ cancer information summary for health professionals provides comprehensive, peer-reviewed, evidence-based information about the treatment of childhood craniopharyngioma. 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.

Reviewers and Updates

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Changes to the summaries are made through a consensus process in which Board members evaluate the strength of the evidence in the published articles and determine how the article should be included in the summary.

The lead reviewers for Childhood Craniopharyngioma Treatment are:

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