Childhood Craniopharyngioma Treatment (PDQ®)
Health Professional Version

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 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

The PDQ childhood brain tumor treatment summaries are organized primarily according to the World Health Organization classification of nervous system tumors.[1,2] 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.

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 follow-up 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 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 newly diagnosed craniopharyngiomas may include a combination of surgery, radiation therapy, and/or cyst drainage. The treatment of recurrent craniopharyngiomas depends on the initial treatment used. The 5-year and 10-year survival rates, regardless of treatment given, are higher than 90%.

Incidence

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

No predisposing factors have been identified.

Anatomy
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.[7]

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, such as germinomas or hypothalamic/chiasmatic astrocytomas, and biopsy or resection is required to confirm the diagnosis.[8]

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

Prognosis

Regardless of the treatment modality, long-term event-free survival is approximately 85% in children,[5,6] with 5-year and 10-year overall survival rates higher than 90%.[9-12]

References

9. Muller HL: Childhood craniopharyngioma. Recent advances in diagnosis, treatment and
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; however, craniopharyngiomas may recur after initial therapy.

Craniopharyngiomas are classified as one of the following:

- **Adamantinomatous**: Adamantinomatous craniopharyngioma is the most frequent type in children. 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. Activating beta-catenin gene mutations are found in virtually all adamantinomatous tumors.

- **Papillary**: BRAF V600E mutations are observed in nearly all papillary craniopharyngiomas. Papillary craniopharyngiomas occur primarily in adults.

References


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. Treatment Options for Childhood Craniopharyngioma

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Treatment Options</th>
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<tbody>
<tr>
<td>Newly diagnosed childhood craniopharyngioma</td>
<td>Radical surgery with or without radiation therapy</td>
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<td></td>
<td>Subtotal resection with radiation therapy</td>
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<tr>
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<td>Primary cyst drainage with or without radiation therapy</td>
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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 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. Radical surgery with or without radiation therapy.
2. Subtotal resection with radiation therapy.
3. Primary cyst drainage with or without radiation therapy.

**Radical surgery with or without radiation therapy**

It may be possible to remove all visible tumor and achieve long-term disease control because these tumors are histologically benign. A 5-year progression-free survival (PFS) rate of about 65% has been reported. 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. Radical surgical approaches include the following:

- **Transsphenoidal approach:** A transsphenoidal approach may be possible for some small tumors located entirely within the sella. The development of expanded endonasal techniques with endoscopic visualization have allowed this approach to be increasingly used, even for sizeable childhood tumors, which is similar to the experience in adults. When an endonasal approach is not possible, a craniotomy is required.

- **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. Almost all craniopharyngiomas have an attachment to the pituitary stalk, and of the patients who undergo radical surgery, virtually all will require life-long pituitary hormone replacement with multiple medications.

<table>
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<tr>
<th>Treatment Group</th>
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<tr>
<td>Recurrent childhood craniopharyngioma</td>
<td>Surgery, Radiation therapy, including radiosurgery, Intradacitary instillation of radioactive P-32, bleomycin, or interferon-alpha, for those with cystic recurrences, Systemic interferon</td>
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Complications of radical surgery include the following:

- Obesity, which can be life-threatening. Hypothalamic-sparing surgical techniques may result in reduced postoperative obesity without an increase in tumor recurrence. [8][Level of evidence: 3iiDi]
- Hormone replacement therapy. [10]
- Severe behavioral problems. [10]
- Blindness.
- Seizures.
- Spinal fluid leak.
- False aneurysms.
- Difficulty with eye movements.
- Death from intraoperative hemorrhage, hypothalamic damage, or stroke (rare).

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. [11][Level of evidence: 3iiiDiii]

Periodic surveillance using magnetic resonance imaging is performed for several years after radical surgery 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 radical surgery. [9]

The surgical procedure is often followed by radiation therapy, with a 5-year PFS rate of about 70% to 90%[4,12]; [13][Level of evidence: 3iDii] and 10-year overall survival rates higher than 90%.[14][Level of evidence: 3iiA]; [15][Level of evidence: 3iiiDiii] Conventional radiation therapy is fractionated external-beam radiation, with a recommended dose of 54 Gy to 55 Gy in 1.8-Gy fractions.[16] Transient cyst enlargement may be noted soon after radiation therapy but generally resolves without further intervention. [17][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 higher PFS rates than was subtotal resection alone. [15][Level of evidence: 3iiDii]

Surgical complications with a subtotal resection are less likely than with radical surgery. 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).[18,19]

Newer radiation technologies such as intensity-modulated proton therapy may reduce scatter.
during whole-brain and whole-body irradiation and result in the sparing of normal tissues. 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.[20-22] It is unknown whether such technologies result in reduced late effects from radiation.[13,21-23]

Tumor progression remains a concern, and it is usually not possible to repeat the radiation dose. In selected cases, stereotactic radiation therapy can be delivered as a single large dose of radiation to a small field.[24][Level of evidence: 3iC] Proximity of the craniopharyngioma to vital structures, particularly the optic nerves, limits this to small tumors within the sella.[25][Level of evidence: 3iiiDii]

**Primary cyst drainage with or without radiation therapy**

For large cystic craniopharyngiomas, particularly in children younger than 3 years and in those with recurrent cystic tumor after initial surgery, stereotactic or open implantation of an intracystic catheter with a subcutaneous reservoir may be a valuable alternative treatment option. Benefits include temporary relief of fluid pressure by serial drainage, and in some cases, for intracystic instillation of sclerosing agents as a means to postpone or obviate radiation treatment. This procedure may also allow the surgeon to use a two-staged 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.[26]

**References**


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:

2. Radiation therapy, including radiosurgery.
3. Intracavitary instillation of radioactive P-32, bleomycin, or interferon-alpha, for those with cystic recurrences.
4. Systemic interferon.

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 less often achieved.[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, to include consideration of radiosurgery in selected circumstances.[4][Level of evidence: 3iiiDiii]

Cystic recurrences may be treated with intracavitary instillation of varying agents via stereotactic delivery or placement of an Ommaya catheter.[5] These agents have included radioactive P-32 or other radioactive compounds,[6,7];[8][Level of evidence: 2A], bleomycin,[9];[10][Level of evidence: 3iiiDiii] or interferon-alpha.[11];[12][Level of evidence: 3iiiB] 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 pegylated interferon alpha-2b to manage cystic recurrences can result in durable responses.[13][Level of evidence: 3iiiDiii]

Treatment Options Under Clinical Evaluation for Recurrent Childhood Craniopharyngioma

The following is an example of a national and/or institutional clinical trial that is currently being conducted. Information about ongoing clinical trials is available from the NCI website.

- **PBTC-039 (NCT01964300)** (Peginterferon Alfa-2b in Treating Younger Patients With Craniopharyngioma That is Recurrent or Cannot Be Removed By Surgery): This is a phase II clinical trial evaluating how well peginterferon alfa-2b works in treating children with craniopharyngioma that is recurrent or cannot be removed by surgery. This trial follows a small (N = 5) single-institution experience with peginterferon alfa-2b, in which prolonged complete responses were observed in some patients.[13]

References

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.

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.[1] Patients with hypothalamic involvement showed impairment in memory and executive functioning.[2]

- Vision loss.

- Endocrine abnormalities. Endocrine abnormalities result in the almost universal need for lifelong endocrine replacement with multiple pituitary hormones.[3-5][Level of evidence: 3iiiC] A report indicated that adults treated with long-term growth hormone replacement after childhood onset craniopharyngioma involving the hypothalamus were at increased risk of cardiovascular disease.[6]

- Obesity, which can be life-threatening, and the development of metabolic syndrome, including nonalcoholic fatty liver disease.[7,8]

- Vasculopathies and stroke. Vasculopathies may result from local irradiation.[9,10]

- Subsequent neoplasms. Subsequent neoplasms may result from local irradiation.[9]

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.

References

1. Winkfield KM, Tsai HK, Yao X, et al.: Long-term clinical outcomes following treatment of


Changes to This Summary (05/17/2016)

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.

Late Effects in Patients Treated for Childhood Craniopharyngioma

Revised the list of late effects of treatment for childhood craniopharyngioma to include stroke (cited Lo et al. as reference 10) and subsequent neoplasms.

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

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Reviewers and Updates
related images, is available in Visuals Online, a collection of over 2,000 scientific images.

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Based on the strength of the available evidence, treatment options may be described as either “standard” or “under clinical evaluation.” These classifications should not be used as a basis for insurance reimbursement determinations. More information on insurance coverage is available on Cancer.gov on the Managing Cancer Care page.

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