Craniopharyngiomas comprise roughly 3% of all intracranial neoplasms and are the most common nonglial brain tumor of childhood, constituting 6 to 8% of all pediatric brain tumors. On a population scale, however, they are relatively rare lesions, with an incidence of only 0.13 per 100,000 person years. Fewer than 350 combined adult and pediatric craniopharyngiomas are diagnosed each year in the United States, and less than half of these occur in children. Thought to arise from embryological remnants of the craniopharyngeal duct, these benign epithelial neoplasms with solid, cystic, and calcified components can arise anywhere along an axis from the third ventricle to the pituitary gland.

The benign histology of craniopharyngiomas, however, belies their rather malignant clinical course in children. Described by Harvey Cushing as “one of the most baffling problems to the neurosurgeon,” their close proximity to the visual apparatus, circle of Willis, pituitary stalk, and hypothalamus predisposes these patients to severe adverse sequelae both at presentation and following treatment. Common findings include headache, vision loss, diabetes insipidus, panhypopituitarism, short stature, hypothalamic dysfunction with behavioral and memory disturbances, hyperphagia, and obesity.

Treatment Philosophy

Debate persists regarding the optimal management of craniopharyngiomas. Regardless of selected management strategy, however, definitive tumor control or cure should be the goal of any treatment for pediatric craniopharyngiomas. Two critical factors for potential cure are extent of surgical excision and cranial irradiation. Some centers advocate radical resection for surgical cure, whereas others favor limited resection followed by radiation therapy to limit injury to the hypothalamus. Both major paradigms provide similar rates of disease control and overall survival. Although radical resection may have a higher potential for immediate perioperative morbidity, limited resection and radiation therapy cause more delayed morbidity, including panhypopituitarism, visual deterioration, cognitive and attentional dysfunction, secondary central nervous system neoplasms, and cerebrovasculopathy, namely moyamoya disease. Palliative procedures, such as stereotactic cyst aspiration and Ommaya reservoir drainage, may provide relief from compression of neural and visual structures, but these effects are invariably transient. Progressive solid and cystic tumor recurrence and growth are inevitable. We believe such therapies should not be considered definitive or adequate treatment early in the course of disease.

The relative scarcity of craniopharyngiomas, the persistent lack of consensus regarding optimal treatment, and the potential morbidity of all forms of treatment combine to make evaluations of the optimal management strategy difficult, if not impossible. Given similar rates of disease control and survival with the two main treatment strategies, the focus of outcome assessment has shifted to quality of life metrics. However, detailed quality of life outcomes from large series of uniformly treated patients are scarce. Here, we describe our preferred treatment paradigm for craniopharyngiomas in children—radical resection with the aim of surgical cure.

Preoperative Evaluation

Depending on the clinical status and age of the patient prior to surgery, we prefer a complete evaluation by various specialists that includes ophthalmologic, endocrinologic, and neuropsychological testing. Parents and families are counseled as to the expected short- and long-term postoperative course.

Our preoperative imaging protocol consists of magnetic resonance imaging (MRI) with frameless stereotactic image acquisition and computed tomography (CT). CT provides
detailed information about the extent and location of tumoral calcification. Careful evaluation of multiplanar MRI is essential to understand the often complex relationship that craniopharyngiomas have to the visual apparatus, hypothalamus, and surrounding vasculature and will lead to improved outcomes.

First, the location of the tumor in relation to the optic apparatus must be determined. Tumors can be entirely subchiasmal primarily within the sella, prechiasmatic with or without subfrontal extension, retrochiasmal involving the floor of the third ventricle and hypothalamus, or have a complex relationship to the chiasm with both pre- and retrochiasmal components. Second, attention must be paid to the relationship of the dorsal aspect of the tumor and the hypothalamus. Increased involvement and deformation of the hypothalamus have been shown to predict the level of preoperative hypothalamic dysfunction, as well as the operative morbidity of resection. Third, as craniopharyngiomas enlarge, they can form multilobulated cysts that extend along the pathways of least resistance and invade nearby anatomical spaces in the anterior, middle, and posterior fossae. These extensions must be recognized to optimize the surgical approach and minimize retraction injury to normal brain parenchyma.

**Surgical Approaches**

Given the variability of the precise location and size of craniopharyngiomas, a variety of approaches have been described by different surgeons. These include the subfrontal, pterional, combined, bifrontal interhemispheric, transcallosal, subtemporal, pterional, transpetrosal, and transsphenoidal approaches.

We prefer a modified pterional exposure that includes removal of the supraorbital rim, anterior orbital roof, and zygomatic process of the frontal bone. This approach provides the shortest, most direct route to the suprasellar cisterns. It minimizes frontal and temporal lobe retraction with wide splitting of the sylvian fissure, allows early release of cerebrospinal fluid (CSF) from the sylvian and carotid cisterns to aid in brain relaxation, and provides early visualization of the carotid arteries and optic apparatus. Tumors extending from the pontomedullary junction to above the foramen of Monro can be successfully and safely removed using this approach without the need for corticectomy, sacrifice of the olfactory nerve, or potential cognitive dysfunction from retraction of both frontal lobes.

Surgical adjuncts include the Cavitron Ultrasonic Surgical Aspirator (CUSA; Tyco Healthcare, Mansfield, Massachusetts), frameless stereotaxy, and rigid and flexible endoscopes and should be used when appropriate. Recently, we have found that endoscopic visualization during dissection of tumor from the ventral surface of the chiasm and floor of the third ventricle greatly enhances the safety of tumor removal in this critical region and allows complete removal of small fragments of tumor and/or calcium deposits that may or may not contain viable tumor cells. The endoscope is also useful for intraventricular visualization and potential resection of tumor that lies within the third or lateral ventricles not accessible via the transsylvian approach. We reserve the transsphenoidal approach for tumors that are primarily or completely within the sella turcica.

**Operative Technique**

Following induction and intubation, patient positioning, and stereotaxy registration, dexamethasone (0.1 mg/kg), phenytoin (15 mg/kg), and cephalexin (25 mg/kg) are administered. Mannitol (0.25 g/kg) is used at the time of skin incision to aid in brain relaxation. The diuretic effect is maximal within 1 hour of infusion and will ideally have its maximal effect at the time of brain and tumor manipulation. Hyperventilation and progressive drainage of CSF from the sylvian and basal cisterns will usually provide excellent brain relaxation, even in the presence of hydrocephalus. Ventricular drainage is reserved for cases refractory to these maneuvers or in cases of severe, increased intracranial pressure unresponsive to medical management. However, if severe hydrocephalus is present or if there is a significant solid tumor component superiorly within the third ventricle, a 4 mm endoscope is placed into the lateral ventricle and held in place with a rigid retractor. This maneuver allows for alternation of visualization and dissection of tumor from the endoscopic, intraventricular, or microscopic transsylvian routes.

A Z-plasty skin incision posterior to the hairline is performed from the tragus to just beyond the midline. The temporalis fascia and muscle are sharply incised with a no. 15 blade and bluntly dissected off the underlying calvarium with a periosteal elevator to allow for excellent reapproximation at the end of the case and minimize temporalis muscle atrophy. A one-piece, modified pterional craniotomy with removal of the anterior orbital roof, supraorbital rim, and zygomatic process of the frontal bone is then performed with the craniotome and chisel and mallet. A brain retractor is used to prevent injury to the orbital contents or lacerate the periorbita during the orbital and supraorbital osteotomies. The dura is dissected from the sphenoid bone, which is removed with rongeurs down to the supraorbital fissure.

The dura is then elevated with a dural hook and incised in a C-shaped fashion. Especially for large tumors that distort the anatomy of or extend beyond the suprasellar cisterns, identification of the vascular anatomy provides critical internal landmarks for safe navigation. Lateral, the sylvian fissure is widely split, and the branches of the middle cerebral artery are identified. The arachnoidal dissection of
the fissure proceeds medially to bifurcation of the internal cerebral artery. Once the carotid artery comes into view, careful inspection of the anterior cerebral artery, optic nerve, chiasm, and/or tracts is performed to understand the relationship of these structures to the tumor (Figs. 6.1 and 6.2).

We caution against early decompression of the cystic portion of the tumor, as this can result in redundancy of the tumor capsule and the overlying attenuated arachnoid. This loss of turgor can obscure the planes of dissection. The overarching strategy for craniopharyngioma resection is to develop an arachnoid plane circumferentially around the tumor within the suprasellar cisterns followed by stalk inspection and possible sectioning. The last and most critical step is manipulation and excision of the dorsal portion of the tumor involving the hypothalamus.

**Fig. 6.1** This 9-year-old girl presented with severe, progressive headache. On examination, the child was found to have a partial left cranial nerve III palsy and 20/40 visual acuity on the left. (A,C) Following administration of gadolinium, magnetic resonance imaging (MRI) revealed a 4 cm, mixed cystic and solid tumor with a postfixed chiasm. (B) Solid calcification in the left suprasellar region was demonstrated on computed tomography (CT). (D) Via right pterional craniotomy, she underwent gross total resection (GTR) of the adamantinomatous craniopharyngioma with transient worsening but eventual improvement in her CN III palsy. Her visual acuity improved to 20/25 following surgery. Despite stalk preservation, she developed diabetes insipidus (DI) and requires DDAVP. She is now 18 years following GTR, has been without disease recurrence and completed graduate school after college.
in the region of the tuber cinereum. Following tumor removal, the entire tumor bed must be inspected for residual disease with either a micromirror or an angled endoscope. Papaverine-soaked Gelfoam pledgets are then placed around the arteries of the circle of Willis to help ameliorate vasospasm (Fig. 6.2) and are removed prior to dural closure.

If the tumor has a significant retrochiasmatic or intraventricular component, the lamina terminalis must be fenestrated (Fig. 6.3). The lamina terminalis is distinguished from the chiasm by its pale, avascular appearance and is often distended and attenuated by the underlying tumor. Tumor within the third ventricle can be delivered simultaneously through the lamina terminalis, as well as from below the chiasm. We find the use of a 4 mm endoscope inserted into the third or lateral ventricle to be extremely helpful to assist in the delivery of the intraventricular component of the tumor, obviating the need for a transcallosal approach to achieve complete resection. For tumors with significant extension into the sella turcica, removal of the tuberculum sellae and posterior planum sphenoidale may be necessary to gain adequate exposure of the intrasellar space. Following tumor removal, all bony defects into the sinuses must be repaired to prevent postoperative CSF fistulas.

**Postoperative Care**

Following surgery and neurologic examination, all children are transferred immediately to the pediatric intensive care unit. A multidisciplinary team of pediatric endocrinologists,
neuro-oncologists, and intensivists collaborate in the postoperative care. Frequent urine and electrolyte analyses are performed to monitor for and aggressively treat electrolyte disturbances, namely diabetes insipidus. Dexamethasone is tapered over the course of 1 week, and Dilantin is continued for 3 weeks following surgery. Dilantin is continued for extended periods only if seizures occur that are not attributable to electrolyte disturbances.

Postoperative MRI and CT are performed within 48 hours following surgery to ensure complete resection. Surveillance MRI and clinical follow-up occur every 3 months during the first year, every 4 months during the second year, every 6 months for the next 3 years, and every year for the next 5 years. Frequent imaging allows for early detection of recurrence while tumors are small and preferably asymptomatic. However, long-term imaging and follow-up are important, as late recurrences have been reported. Regular evaluations by dedicated pediatric endocrinologists, ophthalmologists, and neuro-oncologists are essential in managing these children long term.

Fig. 6.3 (A,B) This 7-year-old boy presented with headache and behavioral outbursts. MRI revealed a 5 cm retrochiasmatic tumor with significant extension into the third ventricle, causing obstructive hydrocephalus. (C,D) Following GTR of his adamantinomatous craniopharyngioma via a right pterional approach and fenestration of the lamina terminalis, he remained neurologically, visually, and hormonally intact, and his hydrocephalus resolved following tumor removal. He did, however, experience slight worsening of his short-term memory but was able to do well in school and currently attends college. He remains disease-free 14 years following resection.
Outcomes and Complications

In the MRI era, radiographically confirmed complete resection is possible in 80 to 100% of patients. Perioperative mortality following aggressive surgery has also declined substantially over the past 2 decades secondary to advances in neuroimaging and microsurgical techniques from over 10% down to 0 to 4% in most current series.3,14–17,20,21,23,31,34,36,53,55,56,66–72 Multiple authors have reported surgeon experience with craniopharyngiomas has a significant impact on the likelihood of achieving complete resection and good functional outcomes;26,34 Surgeons performing more than two operations per year for radical resection had good outcomes in 87% of children compared with only 52% in those performing fewer.26

Numerous centers have reported excellent rates of disease control and functional outcomes with the strategy of radical resection. In a large series by Zucarro,30 complete resection was achieved in 69% of 153 children. All children who underwent complete resection were in school and no more than 1 year behind in grade level, in contrast to only 62% of children who had limited resection and radiation. Di Rocco et al16 reported complete resection in 78% of 54 children treated with curative surgical intent. Overall improvement in intelligence quotient (IQ) occurred following resection in their series with a mean postoperative IQ of 112 (range 95–130). All but 2 of 30 surviving patients enjoy normal social interactions. In a series by Hoffman et al,53 26 of 27 children who underwent aggressive resection had IQ scores at or above average levels. Although 16 children had memory deficits, 14 of them attended regular schools. The authors contended that “memory impairment did not interfere with school progress if intelligence was adequate.” Yasargil et al36 reported good outcomes in 72.5% of children after initial surgery, and Fahrbus et al35 reported functional independence in 78% of adult and pediatric patients following radical resection.

In our series of 86 children who underwent radical resection of craniopharyngiomas, gross total resection (GTR) was accomplished in all 57 (100%) of primary tumors and in 18 of 29 (62%) of recurrent tumors with acceptably low morbidity (Table 6.1). In contrast to the findings of other centers of increased morbidity, mortality, and worse functional outcomes at reoperation,14,20,21,36,55,73–77 we found no such differences in our series. Good and excellent functional outcomes were achieved in 80% of children, and over 60% of college-aged patients either attended or graduated from college—a clear indication of the high functionality of the majority of these children. New hypothalamic morbidity occurred in 25% of children and was mild or moderate in all but one case. Fewer than 20% of our patients developed obesity, and only two patients developed severe or morbid obesity. These results contrast greatly with those from a German multicenter study that reported severe obesity in 44% of 185 children treated for craniopharyngiomas using various treatment modalities.48 Although some centers contend that increasing tumor size limits the extent of resection and local disease control29,31,55,78–84 we agree with other authors30,51,56,85 that size has no impact on the ability to achieve GTR—at least for virgin tumors. Nevertheless, given the large size and multicompartimental nature of giant craniopharyngiomas, a flexible and at times staged approach may be required for successful and safe extirpation of these tumors (Fig. 6.4).

Although our data did corroborate prior studies reporting worse overall survival rates for children with recurrent tumors,25,29,36,55,73,86 subgroup analysis revealed excellent survival rates for children with nonirradiated recurrent tumors and those of smaller size at reoperation. Thus, prior

<table>
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<tr>
<th>Table 6.1 Morbidity and Mortality in 86 Children after Radical Resection of Craniopharyngioma</th>
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<tr>
<td>No. of Patients (%)</td>
</tr>
<tr>
<td>Primary</td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>Perioperative mortality</td>
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<tr>
<td>Neurologic morbidity</td>
</tr>
<tr>
<td>Stroke</td>
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<tr>
<td>Mild hemiparesis</td>
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<tr>
<td>Transient CN palsy</td>
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<tr>
<td>Permanent CN palsy</td>
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<tr>
<td>Lethargy/abulia</td>
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<td>Visual acuity</td>
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<td>Preoperative deficit</td>
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<td>Improved</td>
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<td>Diabetes insipidus</td>
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<td>Preoperative</td>
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<td>Postoperative, new</td>
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<tr>
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<td>Anterior pituitary dysfunction</td>
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<td>Mean number hormones required ± SD</td>
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Note: There were no significant differences in operative mortality, neurologic, visual, or endocrinologic morbidity rates between patients with primary and recurrent tumors (p > .05).

CN, central nerve; SD, standard deviation.
failed radiation therapy and large size at recurrence significantly limited our ability to achieve complete resection—the only remaining option for potential cure for these patients—and resulted in worse overall survival rates. In contrast, prior radical resection, per se, did not diminish the chance of achieving complete resection at reoperation, leading to improved disease control and survival rates. Fourteen children experienced a total of 15 recurrences following GTR at our hospital. All underwent reoperation at the time of recurrence except one child, who had radiosurgery, given the presence of fusiform dilatation of the internal carotid artery. GTR was achieved in 79% with no surgical morbidity or mortality. One patient had slight deterioration in vision, but no child experienced hypothalamic or memory dysfunction. Overall survival for this cohort was 92% at mean follow-up of 8 years, markedly higher than the rate of survival of recurrent tumors reported in the literature.

Recurrence is one of the most common complications of craniopharyngiomas and usually occurs within the first 3 to 4 years following treatment. In modern series, it occurs in roughly 20% of cases following imaging-confirmed complete resection and in 20 to 30% of cases following radiation therapy. These facts must be considered when assessing the efficacy and safety of any treatment algorithm. Thus, in addition to the commonly reported morbidity, one must consider the potentially deleterious effects of early irradiation on the safety and efficacy of subsequent treatments, which prove necessary in up to one third of children. In experienced hands, radical resection alone may afford a greater chance of upfront disease control and potential cure compared with planned limited resection plus radiation and provide more effective and safer treatment options should recurrence arise.

**Craniopharyngiomas in Very Young Children**

The aforementioned risks of radiation therapy are even more common and potentially detrimental in very young children (ages 5 and under). Multiple centers have reported worse functional outcomes, higher rates of tumor recurrence, and decreased overall survival rates in younger children. Importantly, one of the main treatment modalities following subtotal resection (STR) or recurrence—radiation therapy—is usually withheld in very young patients given the age-dependent cognitive morbidity, risk of secondary malignancy, visual deterioration, hypothalamic-pituitary-axis dysfunction, and cerebrovasculopathy, namely, moyamoya disease. In accordance with other centers, we strongly advocate radical resection as the optimal treatment in very young children with craniopharyngiomas.

A retrospective review of our entire series of 86 children revealed 19 children who were age 5 or younger at the time of surgery. GTR was achieved in all but one child, who had undergone numerous prior resections, radiation therapy, and cyst aspirations prior to referral to the senior author for salvage therapy. All remaining (18) patients (95%) were alive at a mean follow-up of 9.4 years. Six children experienced a total of 15 recurrences following GTR at our hospital. All underwent reoperation at the time of recurrence except one child, who had radiosurgery, given the presence of fusiform dilatation of the internal carotid artery. GTR was achieved in 79% with no surgical morbidity or mortality. One patient had slight deterioration in vision, but no child experienced hypothalamic or memory dysfunction. Overall survival for this cohort was 92% at mean follow-up of 8 years, markedly higher than the rate of survival of recurrent tumors reported in the literature.

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patients experienced a total of seven recurrences. Six of these were successfully cured with repeat resection, and the final child had radiosurgery, given the presence of a fusiform dilatation of the internal carotid artery. Four patients had transient cranial nerve palsy, but no permanent neurologic deficits occurred. New cases of diabetes insipidus occurred in 50% of these children, and only one child (6%) experienced visual deterioration. Mean body mass index (BMI) following resection was +1.4 standard deviations and within normal limits. New hypothalamic morbidity occurred in two children (short-term memory impairment and obesity, respectively), and two patients had worsening of their severe hypothalamic disturbance that was present preoperatively. Only 1 of 15 (6.7%) children with normal BMI prior to surgery experienced obesity, and a single patient experienced cognitive deterioration after radical resection. We found no differences in the rates of recurrence, recurrence-free, or overall survival between children ages 5 and younger and those who were older at the time of surgery. No child required conventional fractionated radiotherapy.

Given the increased risk of radiation therapy in young children, we agree with other centers and strongly advocate radical resection as the optimal treatment in very young children with craniopharyngiomas. As our results demonstrate, in experienced hands, excellent oncological and functional outcomes can be obtained in this population with minimal morbidity—sparing this vulnerable population the inherent risks of cranial irradiation.

## Conclusion

We continue to believe that children with craniopharyngiomas should be treated with curative intent at presentation, whether via radical surgery or limited surgery plus irradiation. In accordance with other authors, however, we believe that in experienced hands radical resection of pediatric craniopharyngioma at both presentation and recurrence offers the best chance of a durable disease control and potential cure. Given that most recurrences happen in the first few years following resection and lower morbidity of reoperation on smaller tumors, frequent surveillance imaging in the early postoperative period is necessary to identify recurrence early and immediately treat the tumor while small in size. Late recurrences, however, do occur and require continued long-term follow-up and imaging.

Nevertheless, the conclusions drawn from our experience may not be generalizable to all practices and patients. The success and safety of radical resection depend on surgical expertise, postoperative endocrinologic support, and the familial and societal resources to cope with postoperative care and endocrine and hypothalamic deficits. Educational assistance or tutoring may be required to maintain schooling at appropriate grade level. If family structure and socioeconomic conditions of an individual patient do not provide appropriate support for this chronic disease, the potential morbidity of radical resection may overshadow the merits of curative resection.

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### Subtotal Resection with Adjuvant Therapy

*Frederick A. Boop, David A. Yam, and Thomas E. Merchant*

#### History and Background

Early pioneers in neurologic surgery recognized that tumors in the suprasellar region were challenging to manage. Surgical outcomes were quite poor, and some experts concluded that the region was not to be disturbed by the surgeon. Numerous attempts at both cranial and transsphenoidal approaches continued with occasional success, but for the most part, the results were generally unsatisfying. To make matters worse, these exceptionally rare tumors make up only ~0.8% of all brain tumors, which made experienced surgeons somewhat of a rarity. This problem persists today. Even in the most talented hands, surgical morbidity and mortality rates remain high.

The introduction of corticosteroid therapy in the 1950s revolutionized postoperative management. This was followed by the introduction of desmopressin (trade name DDAVP), which allowed a means to control postoperative diabetes insipidus for the first time. The introduction of the operating microscope and better microsurgical instrumentation to neurosurgery in the 1970s was a milestone that markedly improved survival rates. Because craniopharyngiomas are benign tumors, it was once held that the primary goal of treatment should be a surgical cure by radical resection. The use of adjuvant therapy such as radiation treatment or chemotherapy was eschewed and only offered to patients with recurrent disease or those too sick for a surgical procedure. After decades of reviewing the results of attempted GTR, several neurosurgeons expressed concerns about quality of life and mortality after radical resection.

Thus began a small but growing trend of performing subtotal resection to decompress the optic apparatus and the hypothalamus followed by adjuvant radiotherapy. After a century of improvements in radiographic imaging, pre- and postoperative care, microsurgical techniques, and the addition of adjuvant therapy, the controversies surrounding this rare disease still remain.
Clinical Case 1
A 7-year-old boy presented to his primary care physician offering a 19-week history of nausea, vomiting, and headache. He then developed facial drooping, which prompted evaluation in a local emergency department, where he was found to have a tumor and associated hydrocephalus. His review of systems was positive for decreased visual acuity without a recent change in vision and was negative for symptoms of neuroendocrine dysfunction. His physical exam was remarkable for anisocoria with a dilated but reactive left pupil, decreased acuity on the left eye of 20/200, and a field cut in the left eye. A mild facial droop was present on the left. His exam was otherwise unremarkable. Laboratory studies revealed normal cortisol, prolactin, testosterone, thyroid-stimulating hormone (TSH), free T4 (thyroxine), and antidiuretic hormone but decreased luteinizing hormone, follicle-stimulating hormone, and growth hormone (GH). His radiographic images are included (Figs. 6.5 and 6.6).

Diagnosis and Treatment Considerations
When a child such as this presents with a suspected craniopharyngioma, the neurosurgeon has two major obligations: to obtain a confirmed pathologic diagnosis and to initiate comprehensive treatment. Although radiographic imaging...

Fig. 6.5 Sagittal MRI T1-weighted image with contrast of a 7-year-old boy showing a large sellar and suprasellar mass with cystic regions and radiographic findings consistent with a craniopharyngioma.

Fig. 6.6 Axial MRI T1-weighted images with contrast of the same 7-year-old boy showing the relationship of the tumor to the hypothalamus, the brainstem, and the ventricles.
has dramatically improved over the last few decades, a wide variety of lesions can occur in this region, including craniopharyngioma, pituitary adenoma, epidermoid tumors, optic pathway gliomas, meningiomas, colloid cysts, arachnoid cysts, and inflammatory lesions. For these reasons, biopsy of the mass is almost always indicated except in the most classic cases as confirmed by clinical presentation and radiographic imaging. If the child’s tumor is discovered incidentally, stereotactic biopsy may be the quickest and least invasive method. If, however, there is concern regarding mass effect and neurologic change, open biopsy and resection may be indicated.

For each patient, the treatment should be individualized based on several factors. These include patient characteristics, tumor location, size, preoperative comorbidities, visual function, the presence of hydrocephalus, and hypothalamic pituitary-axis integrity. Each and every issue must be addressed to the fullest extent possible, and the side effects of available treatments must be considered. For tumors with little to no involvement of the anterior hypothalamus such as lesions located within the sella, surgical resection would seem to be a reasonable approach if the surgeon and patient are willing to accept the risk of diabetes insipidus. The more commonly encountered, more extensive tumors with hypothalamic involvement such as the case presented here, however, clearly represent a challenge for the surgeon. Although GTR of large tumors involving the hypothalamus has been performed with success, such success often comes at a high price, leading many to favor an equally effective use of limited surgery and adjuvant radiotherapy.

Radical Resection

Although craniopharyngiomas are histologically benign tumors, the risk of critical adjacent structures being damaged by either the tumor or the proposed treatment remains significant. The surgeon has two main options in the treatment of these tumors: either attempted total resection or subtotal resection supplemented by other therapies to keep the residual tumor from growing. The goal of the radical resection approach is to obtain a surgical cure of this benign disease, thus sparing the patient the risk of radiotherapy. Radical resection can be an effective treatment with excellent rates of long-term progression-free survival. For the experienced craniopharyngioma surgeon, published risks may be acceptable; however, for the average neurosurgeon who has seen only a handful of these tumors in his or her professional lifetime, those statistics do not translate. For tumors involving the hypothalamus, surgical resection has met with severe cost to the patient with a wide range of neuroendocrine and cognitive dysfunction. From the early days of craniopharyngioma surgery to the present, GTR even in highly experienced hands was achievable in only 45 to 75% of cases. As such, a fairly large number of patients with residual disease go on to receive observation, additional surgery, and/or delayed salvage radiotherapy. Recurrence after reported GTR alone without radiotherapy is undeniably common and occurs in up to 53% of cases. Death in patients who undergo attempted radical resection of craniopharyngioma is not uncommon, with a 4 to 9% mortality rate reported in the American Society of Pediatric Neurosurgeons’ survey and higher rates in some series. Morbidity following attempted GTR is an equally significant problem. Of patients with attempted radical resection, up to 96% have a wide range of permanent endocrinopathies related to the operative intervention (Table 6.2). Epilepsy is more frequent in patients managed by attempted radical resection, occurring in up to 40% of patients. Epilepsy is virtually nonexistent in those patients receiving limited surgery followed by adjuvant radiotherapy. In addition, hypothalamic injury sufficient to alter the quality of life is reported in up to 86% of patients undergoing radical resection. Considering these issues regarding mortality, morbidity, residual disease, frequency of recurrence, and quality of life, it is the authors’ opinion that radical resection should be limited to small tumors that do not involve the hypothalamus. Furthermore, given the high recurrence rates in patients with proven GTRs, it behooves us that these patients be followed indefinitely.

Subtotal Resection and Adjuvant Therapy

In contrast to radical resection, the use of subtotal resection and adjuvant radiotherapy aims at maintaining the child’s quality of life by surgically addressing mass effect, tumor volume, and hydrocephalus while halting tumor progression with radiotherapy or other modalities. This approach has been labeled palliative by advocates of radical resection; however, it is clear that this treatment does have proven long-term efficacy at the control of tumor progression equal to that of radical resection. It is also a treatment strategy that is not as dependent upon the skill or experience of the neurosurgeon. Thus, limited surgery followed by focused radiotherapy is a treatment that can be widely applied, whereas radical resection, if it is to be done, should only be done in regional referral centers and by experienced microneurosurgeons with a proven track record. In terms of operative and perioperative mortality, several series have reported patients managed with subtotal resection and adjuvant therapy with no reported deaths. Visual acuity is preserved or improved in the majority of patients using this treatment regimen. In the GTR group, the vast majority of patients suffer from neuroendocrine disorders, whereas patients in the limited surgery and adjuvant treatment group have less early and lower overall neuroendocrinologic dysfunction. This is especially true in regards to cortisol function and diabetes insipidus (Table 6.2). Most
patients following attempted total resection require replacement of GH, TSH, cortisol, and vasopressin. With limited surgery and radiotherapy, hormone dysfunction will exist; however, the avoidance of diabetes insipidus prevents a major cause of death and morbidity in young children with craniopharyngioma.

Although no prospective randomized data are available, large cohort studies do exist looking at the quality of life of patients managed with limited surgery and adjuvant therapy. In these, combined treatment modalities with limited surgery have been shown to have better quality of life outcomes compared with those patients treated by radical resection. In the Boston Children’s series, major disability was found in 33% of radical surgery patients as compared with 15% in those treated with limited surgery and radiotherapy. In the Royal Marsden series of 173 patients treated with limited surgery and radiotherapy, 52% of patients had no disability and lead active lives. This is compared with studies involving radical resection, with up to 80% of survivors describing major disability and impairment. Another cohort of 48 patients treated by either subtotal surgery followed by radiotherapy or radical resection showed that the 62% of patients treated by limited surgery were functional enough to attend normal school versus 37% of those receiving attempted radical resection.

In summary, the use of limited surgery and adjuvant therapy has allowed for improved quality of life with a lower incidence of disability. This has led several regional referral centers to alter their treatment paradigms in favor of limited surgery and adjuvant therapy, including either radiotherapy or chemotherapy. In some centers, the use of intratumoral bleomycin or interferon- has been advocated in younger children to delay more aggressive treatments, including the delaying of radiotherapy.

The use of limited surgery and adjuvant therapy has been proven to prolong survival and control progression of disease. The 10- and 20-year progression-free survival rates reported are 83% and 79%, respectively, in one large series with extended postradiation follow-up. Similar rates of tumor control have been reported at other centers. Considering the improved quality of life, lower incidence of endocrinopathies, comparable rates of vision control, excellent rates of tumor control, and widespread applicability, subtotal resection with adjuvant radiotherapy clearly offers most neurosurgeons and patients a distinct advantage over radical resection.

When using radiation, there are known early and delayed risks that must be considered. Proponents of radical resection are quick to point these out. Earlier studies using conventional opposing beam fields exposed a significant normal brain volume to radiation and its side effects. Improvements in conformal and stereotactic radiosurgery have allowed reduction in these side effects with no diminution in rates of disease control. Documented side effects of radiotherapy have included vasculopathy, cerebral infarction, visual loss, brain necrosis, secondary neoplasia, and neurocognitive sequelae. It should be noted that, although these effects do occur in patients undergoing limited surgery and radiation therapy, many of these side effects also occur in patients treated with radical surgery alone. A common argument against the use of radiation

### Table 6.2 Long-Term Endocrine Deficiencies Following Surgery or Limited Surgery with Radiation Therapy

<table>
<thead>
<tr>
<th>Source</th>
<th>Modality (n)</th>
<th>Thyroid</th>
<th>Adrenal</th>
<th>GH</th>
<th>Gn</th>
<th>DI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tomita (2005)</td>
<td>Radical resection (n = 54)</td>
<td>50 (93%)</td>
<td>50 (93%)</td>
<td>50 (93%)</td>
<td>50 (93%)</td>
<td>47 (87%)</td>
</tr>
<tr>
<td>Poretti (2004)</td>
<td>Radical resection (n = 25)</td>
<td>21 (84%)</td>
<td>19 (76%)</td>
<td>20 (80%)</td>
<td>21 (84%)</td>
<td>23/25 (92%)</td>
</tr>
<tr>
<td>Merchant (2002)</td>
<td>Surgery (n = 15)</td>
<td>15 (100%)</td>
<td>14 (93%)</td>
<td>14 (93%)</td>
<td>4 (27%)</td>
<td>11 (73%)</td>
</tr>
<tr>
<td></td>
<td>Limited surgery + RT (n = 14/15)</td>
<td>14 (93%)</td>
<td>10 (67%)</td>
<td>14 (93%)</td>
<td>8 (53%)</td>
<td>5 (33%)</td>
</tr>
<tr>
<td>Thompson (2005)</td>
<td>Radical resection (25)</td>
<td>NA*</td>
<td>NA*</td>
<td>NA*</td>
<td>NA*</td>
<td>24 (96%)</td>
</tr>
<tr>
<td></td>
<td>Subtotal Resection + RT (n = 23)</td>
<td>NA*</td>
<td>NA*</td>
<td>NA*</td>
<td>NA*</td>
<td>11 (47%)</td>
</tr>
<tr>
<td>Moon (2005)</td>
<td>Limited surgery + RT (n = 25)</td>
<td>-*</td>
<td>-*</td>
<td>-*</td>
<td>-*</td>
<td>10 (38%)</td>
</tr>
</tbody>
</table>

* Data not provided in reference.

Abbreviations: DI, diabetes insipidus; GH, growth hormone; Gn, gonadotropins; RT, radiotherapy.
therapy in children is the development of neurocognitive sequelae. However, as was noted, patients who had had radical resection experience a greater decline in IQ than those managed with limited surgery and radiation. In addition, the use of three-dimensional conformal radiation has reduced the number of complications and the drop-off in IQ. With continued advancements in conformal radiotherapy and stereotactic radiosurgery, these side effects will likely continue to decrease.

Approach to Case 1

Given the patient’s presentation and radiographic findings, this child is likely to have a craniopharyngioma. There is clear hypothalamic involvement, and the cystic regions of the tumor appear to be causing obstruction of CSF flow. The patient’s premorbid conditions include endocrinologic dysfunction, although he does not currently have diabetes insipidus or hypocortisolism, loss of vision in the left eye, and hydrocephalus. Given the lack of acute visual change, this patient does not require emergent or urgent decompression of his optic nerves or chiasm. He does need decompression of his ventricles for treatment of his hydrocephalus, from which he is symptomatic. Because two cystic components are present and contributing to his hydrocephalus, the patient could reasonably be taken to surgery for stereotactic-guided insertion of an Ommaya reservoir, which can be used to aspirate the cyst. The cyst fluid should be sent for cytology, and biopsies can be obtained using framed stereotactic or endoscopic guidance. At the time of surgery, a septum pellucidotomy can be performed, and either a ventricular reservoir or shunt may be inserted for the treatment of hydrocephalus. In this case, the ventricular reservoir is particularly useful, as the CSF obstruction may resolve with the initiation of steroid therapy and adjuvant radiation. This may obviate the need for CSF diversion altogether. Within 24 to 48 hours after placement of the cyst Ommaya and the ventricular Ommaya reservoirs, the patient would likely be ready for discharge. A short time later he could begin adjuvant radiotherapy as an outpatient. Additionally, the use of intratumoral agents is feasible through the Ommaya reservoir. The child will need to be followed long term with serial imaging, neurocognitive assessments, endocrine laboratories, and visual field examinations. Should his tumor progress after treatment, surgical resection would still be a good option, given that all of the arachnoid planes are well preserved.

Clinical Case 2

A 14-year-old male patient presented in coma. He had shown deterioration of his school performance and personality change for 3 months prior to this, but his parents were afraid to question him about it because they were afraid he might be taking drugs. On the morning of presentation, they went to his room to awaken him for school but were unable to arouse him. On presentation he was purposeful to pain. He was in bigeminy with bradycardia and an elevated blood pressure. He had absent reflexes. Following an emergent CT scan, he was moved to the intensive care unit, where bifrontal ventricular catheters were placed. After ventricular drainage, the patient awakened and stabilized. An MRI was performed the next day showing a large cystic and solid suprasellar tumor. His cardiac arrhythmia was felt to be secondary to severe hypothyroidism, which was corrected over 3 to 4 days. He was subsequently taken to surgery.

Discussion of Case 2

This patient was managed with GTR alone. His initial postoperative course was unremarkable and uncomplicated aside from diabetes insipidus. He has panhypopituitarism requiring hormone replacement therapy, including vasopressin therapy to manage his diabetes insipidus. His Glasgow Outcome Scale was a 5, and eventually he was able to return to the public school system to attend classes. According to the Karnofsky Performance Scale, he was independent in his activities of daily living and would perform at nearly 100%. By all the usual measures this patient appeared to have an excellent outcome from his tumor resection. However, these measures do not account for the fact that the child had gone from being a straight A to a C student, with both attentional and behavioral problems. They do not account for the 150 lb weight gain over the next 12 months. They do not account for the fact that he had one useful quadrant of vision in each eye. They do not account for the fact that over the next 3 years a carotid artery pseudoaneurysm developed that necessitated arterial reconstruction. Despite postoperative scans showing a GTR, his tumor recurred in the posterior fossa 3 years later, necessitating a petrosal approach for reresection.

General Discussion

Craniopharyngioma was once treated solely with attempts at GTR, often with unsatisfactory outcomes. Because morbidity and mortality rates used to be unacceptably high, improvements in the management of these patients has focused on reducing these rates and not on true quality of life measures. More sensitive quality of life measures have pointed out major problems in patients managed with attempted radical resection alone. These include abulia, learning and memory impairment, hypothalamic obesity, and social dysfunction, which were not measured in earlier studies. Considering these realities, a treatment paradigm has evolved that not only focuses on mortality and survival rates but also stresses the importance of the child’s quality of life. Due to the rarity and regional referral patterns surrounding the management
of craniopharyngioma, it is unlikely that a prospective randomized trial comparing the two ideologies of treatment could ever be performed. It is likely that there are two subsets of patients with craniopharyngioma: the most common being those with a larger tumor with hypothalamic involvement and the rarer being those with a smaller sellar or suprasellar lesion without hypothalamic involvement. It has been well described that GTR can be performed for patients without hypothalamic involvement; this approach is still widely accepted at many centers, the trade-off being permanent, iatrogenic diabetes insipidus and a higher mortality rate. In using this approach, however, it remains critical that these patients be followed closely for years, given the high rates of endocrinopathy and recurrence. In considering the more commonly encountered subset of patients with tumor that involves the hypothalamus, limited surgery and adjuvant therapy have produced equivalent rates of control with a better quality of life and less dependence on hormone replacement therapy.

It should be acknowledged that craniopharyngiomas occur so rarely that no class I evidence as to best management for all scenarios is available; hence, controversy as to optimal management is likely always to exist. We still do not know what the optimal treatment is for the very young child who presents with headaches, normal visual, and normal hormonal functions. We still do not understand the optimal timing of radiation and/or chemotherapeutic agents. We still do not know what the 20-year follow-up result is for a large cohort of patients who have undergone radiotherapy and limited surgery, although we have several patients who are approaching this duration who appear to be functioning well. We still do not know the long-term effect of growth hormone replacement therapy and its potential effect on regrowth of tumor. With many unanswered questions, it is understandable that craniopharyngioma management has remained controversial. Hopefully, future studies will seek to answer existing questions and many other questions that will lead to continued improvements in patient outcomes.

**Conclusion**

As medical technology advances, the treatment of benign intracranial tumors continues to evolve. The management approaches of cavernous sinus meningiomas and schwannomas are prime examples of how much change is occurring in the field of neurosurgery. The use of three-dimensional conformal and stereotactic radiotherapies has allowed the more precise delivery of radiation while limiting the toxicity to adjacent regions of the brain. Although radiation and chemotherapy have their own associated side effects, these treatments have shown promise in the management of benign disease while maintaining better outcomes than surgical management alone. The combined use of surgery and adjuvant therapy in the management of pediatric craniopharyngioma is a proven strategy that can be applied by neurosurgeons with limited surgical experience with this disease. Perhaps most importantly, this strategy allows for a higher quality of life for children with craniopharyngiomas than in the past when the goal of the surgeon was to resect all of the tumor at all costs. Because of its clear benefits for most patients and the fact that it can be safely instituted in centers with lower clinical volumes, subtotal resection with adjuvant radiation therapy should be considered the best initial treatment for the majority of childhood craniopharyngiomas.

**♦ Lessons Learned**

The philosophy of treatment of craniopharyngiomas has been a classic controversy in pediatric neurosurgery for two generations. It remains a debate as to what level of surgical aggressivity is appropriate and what degree of neurologic and endocrine morbidity is acceptable. As Dr. Wisoff, a proponent of the “aggressive school,” wisely puts it, it is indeed a matter of treatment philosophy rather than the nuts and bolts of scientific evidence. The argument for aggressive surgical resection is best determined by experienced surgeons who serve as referral centers for these rare tumors. This approach which avoids the long term side effects of radiation therapy provides the best opportunity in a potential cure for these locally aggressive tumors. Both groups of authors admit that the role of the experienced surgeon is paramount in achieving a complete resection without a host of functional problems. But beyond the small number of surgeons experienced in resecting this rare tumor, how is experienced to be measured?

Dr. Boop’s group strongly point toward the significant morbidity, even considerable mortality, of attempts to remove craniopharyngioma completely. The fact that we even must take mortality seriously into account is uncomfortable. Massive rates (up to 86%) of hypothalamic dysfunction affecting the quality of life lead them to advocate a more conservative philosophy. They argue that an attempt for radical resection should only be made if the hypothalamus is not significantly involved in the tumor growth. Those where the hypothalamus is infiltrated should be treated by debulking surgery alone with the explicit aim to maintain the child’s quality of life. Adding radiotherapy to this conservative surgical approach maintains a sufficient tumor control comparable to that achieved by radical resection.
Intracranial involvement. Centers, at least those patients who have hypothalamic involvement. simple biopsies but rather conservative tumor resections. reducing the radiation field. These surgeons do not advocate "leaving something behind." Given the fact that not all patients will ever be treated by the handful of most experienced craniopharyngioma surgeons, and given the, in our view, very acceptable long-term survival rate of patients treated with conservative resection and radiotherapy, the latter approach will work well for more patients than will the radical surgery philosophy.

References
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