Childs Nerv Syst (2005) 21: 785–789
DOI 10.1007/s00381-005-1225-2

SPECIAL ANNUAL ISSUE

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Craniopharyngiomas of childhood: the CHLA experience

Received: 4 May 2005
Published online: 18 June 2005

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Abstract *Objective:* To improve the outcome of children with craniopharyngiomas by analyzing how they were treated. *Methods:* The records of patients who underwent operation at Childrens Hospital of Los Angeles (CHLA) from 1993 to 2004 were reviewed. *Results:* Identified were 19 girls and 16 boys with an age range from 9 days to 16 years (mean 7 years, mode 3 years). Tumor control was achieved in 34 of 35 patients and was accomplished with reasonable outcome in terms of neurological deficits and overall level of function. In 25 patients, complete tumor resection was obtained with surgery alone, 18 with the first resection, and 7 with repeat operative intervention. Nine children received radiation therapy after the first or second recurrence. On retrospective review, there were no consistently identifiable features that would lead one to determine preoperatively which tumors would fall into a given category. *Conclusion:* We believe that the surgeon must determine a preoperative plan that maximizes the chance for a gross total removal of the craniopharyngioma. The biggest challenge intraoperatively is to determine whether to continue with the attempt at gross total removal or stop short of that goal before producing a significant irreversible neurological deficit. A staged removal using different operative corridors also needs to be considered.

Keywords Craniopharyngioma · Brain tumor · Surgical approach · Radiation therapy · Outcome

Introduction

Craniopharyngiomas represent the most common nonglial intracranial tumors of childhood. They arise from epithelial nests that are believed to be embryonic remnants of Rathke's pouch. Their location on an axis extending from the sella turcica along the pituitary stalk to the hypothalamus and floor of the third ventricle explains both their associated symptoms and the difficulties of treatment. Thus, although the histology is benign, the clinical course is not. This is especially true in children, given the importance of an intact hypothalamic–pituitary access for growth and development.

Considerable controversy exists regarding the management of these tumors, with the treating physician having to weigh a slowly inexorable progression of disease with the possible high morbidity and mortality of treatment and its attendant sequelae. With this in mind, many physicians have advocated multimodal therapy, usually involving some combination of radical resection, radiation therapy (RT), and intracystic chemotherapy [3–5, 7]. The treatment of craniopharyngiomas at Childrens Hospital of Los Angeles (CHLA) has been marked by an initial surgical approach to remove as much tumor as safely possible, followed by RT as an adjuvant where indicated.

Materials and methods

A retrospective record review was conducted on all patients treated surgically for craniopharyngioma at CHLA between January 1, 1993, and September 30, 2004. Forty three such patients were identified. Seven patients were excluded due to lack of follow-up information. One pa-

tient was excluded because the initial surgical management was elsewhere. A total of 35 patients whose first microsurgical tumor removal was performed at this hospital were selected. Their charts were reviewed, with specific attention to sex, age, presenting symptoms, tumor size, surgical approaches, and most recent follow-up evaluation.

Results

Demographics

The study included 19 girls and 16 boys. Age at the time of surgery ranged from 9 days to 16 years (mean 6.7 years, mode 3 years). Fourteen patients (40%) were between 5 and 10 years.

Presenting signs and symptoms

Headache was the most common presenting symptom and was seen in 23 patients. Sixteen patients showed evidence of visual disturbance, with blurred vision and diplopia as the most common symptoms. One patient had monocular hemianopsia.

All patients underwent endocrinologic workup preoperatively. Five patients had evidence of endocrinopathy. All five of these had elements of diabetes insipidus (DI). Four patients presented with growth failure. One patient had panhypopituitarism on preoperative evaluation.

In one patient, the lesion was detected through a routine prenatal ultrasound.

All patients but one underwent both magnetic resonance imaging (MRI) and computerized tomography (CT) on initial evaluation.

Tumor size

The tumors ranged in size on preoperative imaging from small (2×2×1 cm) to large (6×7×4 cm). These dimensions included the cyst wall for cystic tumors.

Surgical approach

In all cases, a surgical approach was tailored to allow the possibility of maximal tumor resection. However, the association of tumor with the third ventricle and/or optic apparatus oftentimes limited the extent of the resection. Twenty nine of the 35 patients had a gross total excision of their tumor by surgeon's estimate and confirmed by postoperative imaging.

Open craniotomy was used in 31 patients. A subfrontal approach was used in 11 patients with midline low-lying tumors. In eight of these patients, the approach was bifrontal; in three patients, a unilateral right frontal approach was used.

A transcallosal approach was used in seven patients who had tumor extension superiorly into the third ventricle. A pterional approach was used in five patients who had limited extension into the anterior third ventricle, with the bulk of the tumor centered in the sellar and suprasellar areas.

Combined approaches were used in eight patients for maximal surgical resection. A combined transcallosal and subfrontal approach was used in three patients who had bulky disease in the suprasellar area and large cysts extensively into the third ventricle. A subfrontal and pterional (extended pterional) combination was used in five patients who had bulky disease in the chiasmatic region.

Four patients underwent transsphenoidal craniotomy for disease limited to the sellar and suprasellar regions. This approach was effectively used in a patient as young as 8 months.

Surgical follow-up

Follow-up ranged from 1 to 11 years, with a mean of 4.6 years. All patients had at least MRIs at 3 months and 1 year postoperatively.

There was one death 3 months postoperatively, It was of an infant who was diagnosed prenatally. He died after a subtotal resection (Fig. 1). Surgical morbidity was seen in 9 of the 35 patients and included 6 worsening visual deficits, 4 new cranial nerve deficits, and 3 cortical strokes.

As was previously noted, six patients had residual disease after the first surgery. One of these patients, a 9-day-old child on presentation, died after surgery. He presented with the massive tumor seen in Fig. 1. One patient has had stable disease at less than 2 years and has required no further intervention. One patient with residual disease underwent a second surgical resection and will be considered below. The three other patients with residual disease all received RT.

Twelve patients with initial gross total resections recurred between 2 months and 10 years (mean 24 months) after their initial surgical procedure. One of these patients presented with headaches 2 months after the initial procedure. However, the other 11 remained asymptomatic, and the recurrence was detected on surveillance scanning. Ten of these recurrences were treated with repeat surgical resections. The most common site of recurrence was sellar/suprasellar; thus, pterional craniotomy was used in most cases, although three patients underwent transsphenoidal craniotomy. The remaining two recurrences were treated with RT.

Three patients had residual disease after the second surgery. One of these patients had persistent sellar disease. This residual disease was treated with a transsphenoidal

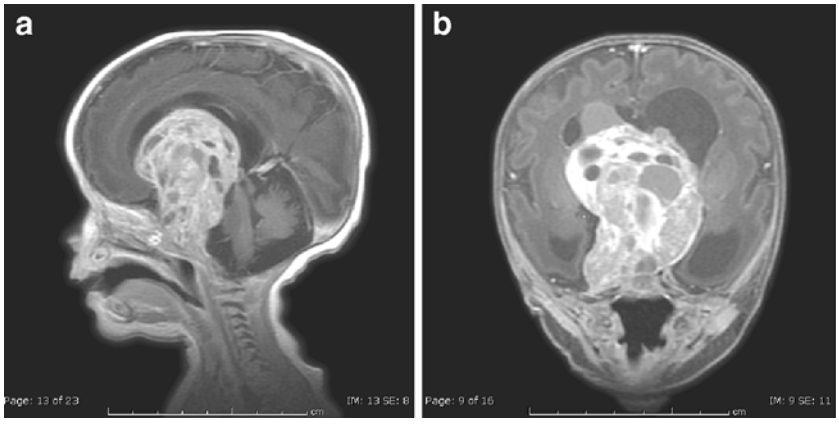

Fig. 1 Contrast-enhanced **a** sagittal and **b** coronal MRIs of a 9-day-old baby boy with third ventricle tumor diagnosed on fetal ultrasound. Patient underwent endoscopic biopsy, which was histologically a craniopharyngioma. One week later, a transcallosal approach was used for tumor resection. The tumor bled excessively, and after replacing the neonate's blood volume three times, an attempt was made to stop the bleeding with aprotinin, to which the patient developed an immunologically proven anaphylactic reaction, at which point the operative procedure was terminated. Patient died 3 months after the surgery having never regained consciousness

craniotomy and has not recurred at 42-month follow-up. Two of these patients underwent RT.

Four patients had a second recurrence at a mean time of 26 months. All of these recurrences were detected on surveillance imaging. One patient was treated with RT. Two patients underwent a pterional craniotomy (one patient had a combine subfrontal/pterional approach for the first surgery and a transsphenoidal for the second, and the other patient had a transsphenoidal as first surgery and a pterional for the first recurrence). The third patient had a transsphenoidal approach for the third surgery (after a pterional craniotomy for the initial surgery and a subfrontal craniotomy for the second surgery). All of these recurrences were in the suprasellar area.

For these three patients with second recurrences treated surgically, two have shown no evidence of disease recurrence at more than 2-year follow-up. One patient had a recurrence at 3 years and has received RT.

Radiation therapy

Nine patients (out of 35) received RT. Eight patients received focused beam RT, and one patient received stereotactic RT. Five patients received the RT after the first surgery. Three of these patients had subtotal resection initially. The remaining two patients received RT almost 2 years after the surgery due to recurrence. In four of these five patients, the tumor cyst progressed in the first year after the RT. These patients underwent a repeat surgical resection of the cyst and have since shown no evidence of disease progression. Three of these patients underwent an open craniotomy; one underwent a transsphenoidal approach due to growth of a suprasellar cyst (Fig. 2).

In three patients, the RT was given after the second surgery. One patient showed no recurrence of tumor at 3 years, and the other two have remained stable with limited follow-up.

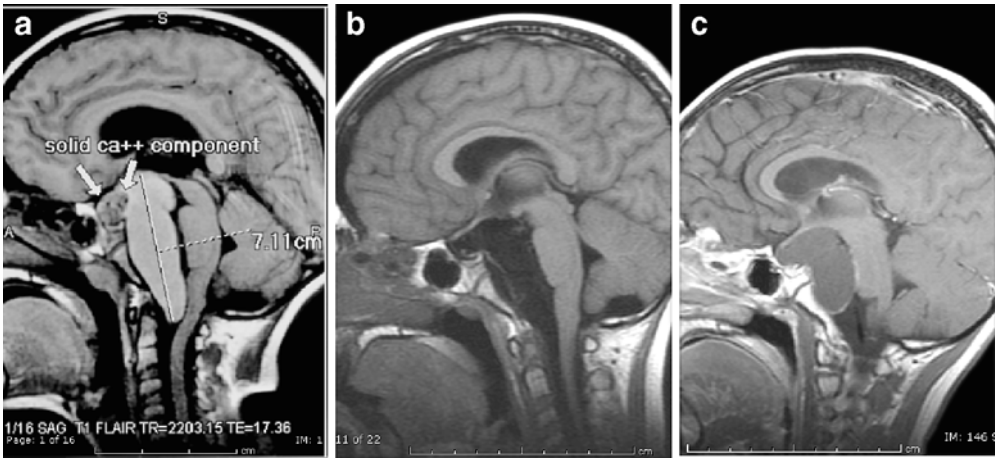

Fig. 2 Nine-year-old patient with **a** sellar lesion extending into the posterior fossa. **b** Postoperative sagittal MRI. Inasmuch as the tumor capsule was intimately attached to the basilar artery, further attempt of removing it was discontinued and RT was given. **c** Five months after the radiation, the cyst recurred, requiring operative intervention with drainage

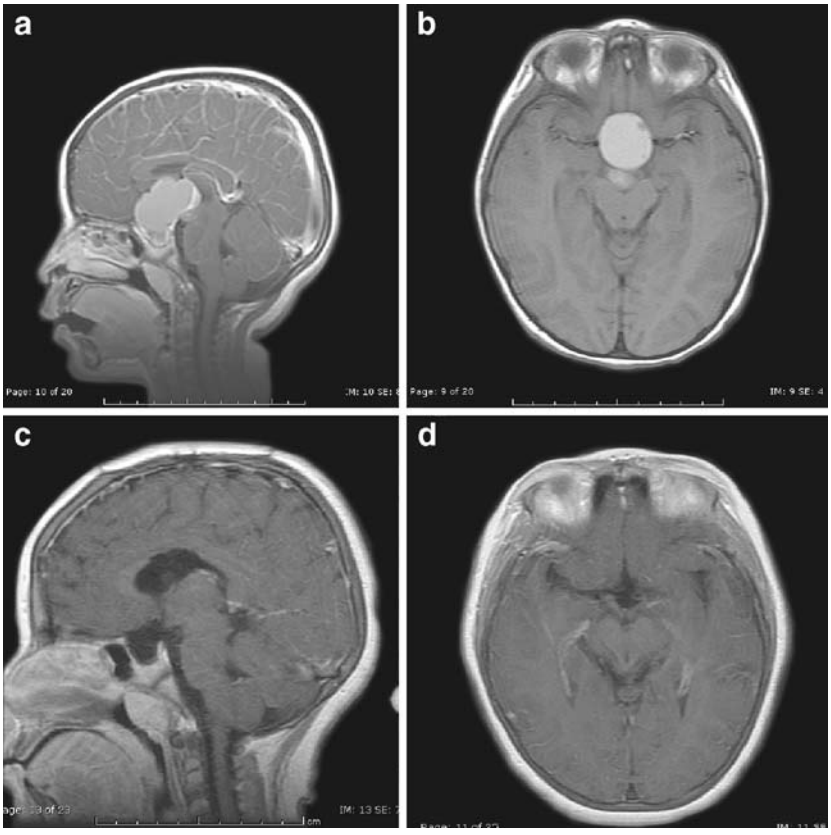

Fig. 3 Seven-year-old patient with **a**, **b** craniopharyngioma filling the sella and extending into the third ventricle. **c, d** Follow-up MRI 3 years after surgery showing no recurrence nor residual tumor

One patient received RT after the third surgery. This patient has no evidence of disease progression at 42 months.

Endocrine function

Endocrine status was evaluated postoperatively in all 35 patients. No patient had normal hypothalamic–pituitary function. Twenty seven patients developed DI, requiring DDAVP, in addition to the five patients who had DI preoperatively. Thirty one patients eventually required cortisone replacement, and 26 required thyroid hormone replacement. Twenty three children showed evidence of panhypopituitarism.

School performance

Data on school performance were available on 30 patients. Twenty four patients were at grade level, with or without resource room instruction. Five patients received special education due to visual or neurologic compromise. One patient is in a chronic care facility with significant neurological deficits.

Discussion

The management of childhood craniopharyngioma remains controversial. The improvement of surgical techniques, including the use of advanced surgical adjuvants and the recognition of appropriate surgical approaches, has reduced morbidity and mortality and improved the efficacy of resection. Most would agree that the best chance to definitively cure the disease is at the time of the first surgery [6, 9]. However, surgery can also result in the most egregious damages to the patient. This fact, combined with the advances in the delivery of RT, advocates for a judicious surgical intervention [1, 2]. Data suggest that, when a complete surgical extirpation is not possible, an acceptable treatment is subtotal tumor resection followed by RT [4].

At CHLA, total excision of the tumor when safe has been the goal of treatment (Fig. 3). This current series includes children treated over the last 11 years using microsurgical techniques, modern neuroimaging, and endocrinological management. All of our patients have been followed with serial surveillance MRIs to detect recurrences early.

Several lessons can be drawn from this series. The first is that the initial surgical attempt for a gross total removal is the best chance for cure where appropriate. Eighteen of the 35 patients have been classified as cured based on their initial surgical resection. These patients on the whole did well, with an acceptable morbidity rate.

However, the surgeon must be able to recognize when cure is not possible during the first surgery before causing significant irreversible damage. Disease control was obtained in the other 16 patients with subtotal resections or recurrences (excluding the one mortality) through 18 additional operative procedures and nine applications of focused radiation.

The use of an appropriate operative approach is necessary for achieving the greatest tumor removal with the least morbidity. A transcallosal corridor gives good exposure to tumor, especially the cystic component in the third ventricle, and it allows good visualization of the tumor–hypothalamus interface. The disadvantage is that residuals can remain in the sellar and infrachiasmatic regions. A transsphenoidal craniotomy was also frequently used to remove tumor in the sellar and suprasellar regions. In the current series, it was used ten times for four initial procedures and in six cases of recurrence. When used appropriately, this approach can be very efficacious; it resulted in cure, seven out of the ten times.

Radiation therapy was also useful for localized areas of solid tumor recurrence. In five of the nine cases where it was given, no tumor progression was seen. However, four cases of cystic tumor had subsequent cyst growth after therapy, requiring repeat surgical resection. Of note is that, in all of these cases, there was no further growth of the irradiated solid component after the cyst was removed. Our series is too short-termed to fully evaluate the long-term consequences of RT. However, it is expected that, as these techniques of applying radiation improve, the morbidity of such therapy will be further reduced while enhancing its efficacy, which in turn will lead to increased use [8].

Postoperative endocrine disturbances frequently occur after total or near total resection. Yasargil et al. [9] identified the pituitary stalk in 51% (of pediatric cases) and could only preserve the stalk in 28%. But in spite of stalk preservation, two thirds of these patients developed DI. Endocrine deficiency was present in all our patients after surgery, including subtotal resection. Twenty three patients required three or more replacement hormones. However, modern endocrinological management has allowed them to live well and keep their hypopituitarism well regulated.

For patients with this histologically benign tumor, the quality of life is important. Unfortunately, sophisticated neuropsychological testing was not undertaken in all of our patients, and no uniform accounting was made of obesity. However, the limited data in this series show a very reasonable outcome, similar to other reported series. Eighty percent of these patients are receiving age-appropriate schooling.

In conclusion, disease control was achieved in 34 out of 35 patients in this series. This was accomplished with a reasonable outcome in terms of neurological deficits and overall functioning. In 25 of these patients, disease control was obtained with surgery alone: 18 on first resection and 7 with repeat resections. Nine patients received RT after the first or second recurrence. On retrospective review, there were no consistently identifiable features that would lead one to determine preoperatively which tumors would fall into any of these categories. Thus, we believe that the surgeon must determine an operative plan that leads to the best chance of cure. The biggest challenge is intraoperatively determining whether to continue to remove tumor before causing significant irreversible neurological damage.

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