Adult craniopharyngiomas: surgical results with a special focus on endocrinological outcomes and recurrence according to pituitary stalk preservation

Clinical article

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Object. The aim of this study was to evaluate the results of surgical treatment of adult craniopharyngioma with a special focus on the endocrinological outcomes and tumor recurrence in cases of pituitary preservation.

Methods. Between 1993 and February 2008, 41 patients underwent 47 surgical procedures for craniopharyngioma. The male/female ratio was 26:15 and the median age was 45.8 years (range 17–65 years). The median follow-up period was 10.56 years (range 6.2–14.9 years). Patients presented with visual disturbance before 30 (63.8%) of 47 procedures and with endocrinological disturbance before 12 (26%) procedures. Surgery was performed via a subfrontal/pterional approach in 31 procedures (66%), bifrontal interhemispheric in 6 (12.8%), transcallosal/transventricular in 5 (10.6%), combined in 1 (2.1%), and transsphenoidal in 4 (8.5%). The tumor was totally removed in 36 procedures (76.6%), subtotally in 10 (21.3%), and partially in 1 (2.1%).

Results. Postoperatively, the rates of visual improvement and aggravation were 50 and 33.3%, respectively. Of 24 patients in whom the pituitary stalk was preserved, complete hormone replacement was needed in 14 (58.3%), partial replacement in 2 (8.3%), and no replacement in 8 (33.3%). The rate of tumor recurrence was 24.4%. The recurrence-free survival rate was significantly different between patients in whom complete tumor resection was accomplished and those in whom tumor resection was incomplete. Stalk preservation did not affect the recurrence-free survival rate. The morbidity and mortality rates were 8.5 and 2.1%, respectively.

Conclusions. The pituitary stalk must be preserved with maximal tumor resection whenever possible to increase the chance of intact anterior pituitary function being maintained. The results of the present study show that pituitary stalk preservation may not be related to increased recurrence rates. (DOI: 10.3171/2008.10.JNS0880)

KEY WORDS • craniopharyngioma • endocrine function • pituitary stalk

CranioPharyngioma is usually a benign CNS tumor. Despite its benign nature, craniopharyngioma remains challenging because of the tumor’s proximity to vital structures, including the optic apparatus, pituitary stalk, hypothalamus, and vessels in the circle of Willis, and therefore the treatment of these tumors can be quite difficult. Total resection is the basic surgical approach for craniopharyngioma, especially in young patients; aggressive surgery, however, is associated with a high risk. In addition, the high frequency of regrowth and recurrence associated with this tumor is a challenge for neurosurgeons during long-term follow-up periods, and the recurrence rate at 10 years is ~ 19%, even in patients in whom apparent gross-total resection is performed.

Preoperatively, craniopharyngioma causes symptoms in 3 different ways: 1) by increasing the pressure on the brain, 2) by disrupting the function of the pituitary gland, and 3) by damaging the optic nerve. The increased pressure on the brain causes headache, nausea, vomiting (especially in the morning), and difficulty with balance. Damage to the pituitary gland causes hormonal imbalances that can lead to excessive thirst and urination, diabetes insipidus, and stunted growth. Vision problems develop when the optic nerve is damaged by the tumor. These defects are often permanent and may worsen after surgery to remove the tumor. Most patients have at least some visual defects or evidence of decreased hormone production at the time of diagnosis. A significant percentage of patients have long-term hormonal, visual, and neurological problems following the treatment of craniopharyngioma.

It is generally believed that craniopharyngioma surgery results in a high rate of hypothalampituitary dysfunction. The intraoperative handling of the pituitary stalk and pituitary gland fundamentally affects endo-

This article contains some figures that are displayed in color online but in black and white in the print edition.
crine function. This retrospective study focuses on the surgical treatment of craniopharyngioma with a special focus on the endocrinological outcomes and recurrence. We reviewed cases of surgically treated craniopharyngioma involving patients older than 17 years of age who presented to our institute over a 15-year period and analyzed the percentage of functional stalk preservation and the rate of recurrence after anatomical stalk preservation at surgery.

Methods

Patient Population

Between 1993 and February 2008, 41 patients underwent 47 surgeries for craniopharyngioma in our department. Twenty-six of the patients were male and 15 female, and their ages at the time of surgery ranged from 1 to 65 years (median 45.8 years).

Neuroradiological assessment was performed with CT or MR imaging before the operation. The tumor was characterized by type (predominantly cystic, solid, or mixed) and location (completely suprasellar, largely suprasellar with a smaller intrasellar component, purely intrasellar, or purely third ventricle).

The goal of surgery was excision of as much of the tumor as possible without incurring neurological or neuropsychological complications. We attempted to preserve the pituitary stalk whenever possible. In 43 of the procedures, patients underwent craniotomy—subfrontal or pterional, bifrontal interhemispheric, transcallosal/transventricular, or combined (transcallosal and pterional) approaches—and only 4 patients with intrasellar tumors underwent transsphenoidal surgery. Within 3 months after surgery, all patients underwent neuroradiological studies as a part of their reassessment. All patients underwent routine neuroimaging studies every 6–12 months as well as monthly clinical examinations.

Total resection was defined as no residual tumor left behind, as determined by both both intraoperative assessment and on postoperative neuroimaging (both CT scans and MR images). Subtotal resection was defined as small but definite signs of residual tumor seen intraoperatively or on neuroimages. Small flecks of calcification observed to have been left behind on postoperative CT scans were deemed to be residual tumors. Partial resection was defined as the finding of a definite residual tumor both intraoperatively and on neuroimages. The decision to perform subtotal or partial tumor removal was made by the surgeon during the operation, based on the difficulty of each surgery.

Clinical information on each patient was obtained by reviewing their medical records. The median follow-up period was 10.56 years (range 6.2–14.9 years). The clinical data, including presenting complaints, radiological findings, surgical approaches, extent of resection, stalk preservation rate, visual and endocrinological outcome, and recurrence rate, were analyzed.

Endocrinological Evaluation

Endocrine function was assessed preoperatively and at 2 weeks after surgery. In patients with pituitary stalk preservation, dynamic stimulation was performed postoperatively for the evaluation of anterior pituitary function.

Basal plasma concentrations of adrenocorticotropic hormone, cortisol, thyrotropin-releasing hormone, thyroxine, luteinizing hormone, follicle-stimulating hormone, prolactin, growth hormone, and somatotropin-C were assessed preoperatively. A combined anterior pituitary stimulation test was performed postoperatively to study pituitary function in patients with stalk preservation. The test was conducted using 5 units of regular insulin, 400 μg of thyrotropin-releasing hormone, and 100 μg of luteinizing-hormone releasing hormone, all administered intravenously. The hormone levels were checked immediately and 15, 30, and 60 minutes later, and the results were compared with the normal range of response. Posterior pituitary function was assessed by monitoring fluid intake and urine output, with measurement of the specific gravity of the urine, for at least 14 days postoperatively.

Ophthalmological Evaluation

The ophthalmological findings of visual acuity and visual fields were analyzed according to the method described by Fahlbusch and Schott. The scores for visual acuity and visual field defects in each patient were added to obtain the visual impairment score, which allowed for an exact comparison between the results of different examinations in each patient.

Statistical Analysis

Comparisons between visual outcome groups were made using the Wilcoxon signed rank test. The cumulative probability of recurrence was estimated as a function of time after surgery using the Kaplan-Meier survivorship method. Comparisons of survivorship curves were made with a generalized Wilcoxon method. Statistical analysis was performed using the SPSS software program (version 16.0 for Windows, SPSS Inc.).

Results

Endocrinological Outcome According to Stalk Preservation

Four of the 41 patients underwent radiation therapy—2 patients immediately after first operation and 2 after a second operation. We analyzed data pertaining to a total of 39 patients after the exclusion of 2 patients who received radiotherapy immediately after the first operation.

Of the 39 patients, 29 (74.4%) received total HRT with prednisolone, levothyroxine, and desmopressin, and 2 (5.1%) received partial HRT with prednisolone and levothyroxine. Eight patients (20.5%) showed intact pituitary function.

The stalk was preserved in 24 of 39 patients, and stalk section was performed in 15. All 15 patients in whom stalk section was performed had endocrine dysfunction (100%). Of the 24 patients in whom the stalk was preserved, 14 (58.3%) received total HRT and 2 (8.3%) received partial hormone replacement. Eight (33.3%) patients showed intact pituitary function (Table 1).
Of the 24 patients in whom the stalk was preserved, total resection was achieved in 18, and subtotal or partial removal was performed in 6. Of the 18 patients in whom total removal was performed with stalk preservation, 11 (61.1%) received total HRT, 1 (5.6%) received partial replacement therapy, and 6 (33.3%) showed intact pituitary function. Of the 6 patients in whom subtotal or partial removal was performed with stalk preservation, 3 (50%) received total HRT and 1 (16.7%) received partial replacement. Two patients (33.3%) showed intact pituitary function (Table 2).

Only 6 patients (of 39) underwent total resection and had an intact stalk and normal pituitary function.

Relationship Between Recurrence/Regrowth and Stalk Preservation and Extent of Removal

We analyzed data pertaining to 39 patients, after the exclusion of the 2 patients who received radiotherapy immediately after the first operation. Recurrence or regrowth of tumor was seen in 10 of 39 patients in this case series, for an overall recurrence and regrowth rate of 25.6%. Actuarial recurrence-free survival rates at 1, 3, 5, and 8 years were 91.5, 84.5, 78, and 46.8%, respectively. Figure 1 shows the Kaplan-Meier survival analysis of our patients.

Thirty of the 39 patients underwent total tumor removal and 9 underwent subtotal or partial tumor removal in the initial surgical procedure. When tumor regrowth and tumor recurrence were considered separately based on the neuroimaging findings after the primary surgery, recurrence after total tumor resection was observed in 7 (23.3%) of 30 patients, and regrowth after incomplete resection and partial resection was observed in 3 (33.3%) of 9 patients. We analyzed the relationship between recurrence and the extent of the surgical removal of the tumor. There was a significant difference in the recurrence-free survival rate between the patients in whom complete tumor resection was achieved and those in whom tumor resection was incomplete (p = 0.023) (Fig. 2).

We analyzed the relationship between stalk preservation and recurrence rate in the 39 patients who underwent total tumor resection and did not receive radiation therapy. The stalk was preserved in 24 patients, and stalk section was performed in 15 patients. The recurrence rate was 25% (6 of 24 patients) in the patients in whom the stalk was preserved and 26.7% (4 of 15) in the patients who underwent stalk section. There was no statistically significant association between stalk preservation and recurrence-free survival (p = 0.67) (Fig. 3).

Ten of the 41 patients who were treated with primary surgery in our department experienced recurrence during the follow-up period. Six patients underwent a second operation for tumor recurrence, and 2 of these patients received radiotherapy immediately after the second surgery. Radiosurgery was performed in 3 of the other 4 cases, and 1 patient remained under observation.

Presenting Complaints and Radiological Findings

Patients presented with visual disturbance before 12 (26%)—hyperprolactinemia was identified before 13% of the procedures, diabetes insipidus before 10.9%, and hypothyroidism before 2.1%. Other presenting symptoms included headache (26% of procedures) and cognitive impairment (2.2%).

In 31 procedures (66%) a complete suprasellar mass was found, and in 9 (19.1%) a large suprasellar mass with a smaller intrasellar component was found. In 2 procedures (4.3%) purely intrasellar masses were found, and in 5 (10.6%) purely third ventricle masses were found. A mainly cystic mass was found in 25 procedures (53.2%), a mixed mass in 14 (29.8%), and a solid mass in 8 (17%).

Surgical Approaches and Extent of Resection

A subfrontal andpterional approach was the approach used most frequently in our series, and it was exclusively applied in 31 procedures (66%). Other approaches used included a basal bifrontal interhemispheric approach in 6 procedures (12.8%), a transcallosal transventricular approach in 5 procedures (10.6%), a transphenoidal approach in 4 (8.5%), and a combined (transcallosal and pterional) approach in 1 (2.1%). Total resection was achieved in 36 procedures (76.6%), and subtotal removal was performed in 10 (21.3%). Partial resection was performed in 1 procedure (2.1%).

Histopathological examination showed an adamantinomatous type craniopharyngioma in 30 patients (73.2%) and a papillary type craniopharyngioma in 11 patients (26.8%).

The early surgical mortality rate for the 47 procedures was 2.1%. One patient died of brain swelling due to seizure 3 days after surgery. The operative morbidity rate was 8.5%. Most complications were controlled without sequelae. After transcranial surgery, 2 patients had post...

| Table 1: Postoperative pituitary function in 24 patients in whom the stalk was preserved and 15 in whom stalk section was performed |
|---------------------------------|-----------------|-----------------|
| Pituitary Function | Stalk Preservation | Stalk Section |
| sacrificed | 14 (58.3) | 15 (100) |
| partially sacrificed | 2 (8.3) | — |
| preserved | 8 (33.3) | — |
| total no. of patients | 24 | 15 |

| Table 2: Postoperative pituitary function and extent of pituitary removal in 24 patients in whom the stalk was preserved |
|---------------------------------|-----------------|-----------------|
| Pituitary Function | Complete Removal | Incomplete Resection |
| sacrificed | 11 (61.1) | 3 (50) |
| partially sacrificed | 1 (5.6) | 1 (16.7) |
| preserved | 6 (33.3) | 2 (33.3) |
| total no. of patients | 18 | 6 |
operative hemorrhages that required surgical evacuation, and 1 patient had transient cranial nerve III palsy. Meningitis was found after transsphenoidal surgery in 1 case, and ventriculoperitoneal shunting was performed.

Visual Outcomes
We reviewed 30 procedures for which patient’s visual impairment scores could be calculated. The patients’ preoperative visual impairment scores were compared with their postoperative impairment scores. After 15 procedures (50%) there was improvement after surgery. Visual deterioration occurred after 10 procedures (33.3%), and 5 (16.7%) resulted in no change in vision. The mean preoperative visual outcome score was 56.2 and the mean postoperative visual outcome score was 49.8. However, there was no statistically significant difference between the pre- and postoperative visual impairment scores (p = 0.424) (Fig. 4).

Discussion
Postoperative Endocrinological Findings Associated With Pituitary Stalk Preservation
After surgery for craniopharyngioma, a high rate of postoperative pituitary deficiency and even of panhypopituitarism has been reported in surgical series. Yasargil et al., who performed radical excision in all cases, observed permanent diabetes insipidus in 98.7% of their patients. However, the preservation of > 50% of anterior pituitary function was accomplished by Baskin and Wilson, who reported on a mixed transcranial/transsphenoidal series. The pituitary stalk is a crucial structure in craniopharyngioma surgery because it is the structure from which the tumor often originates. Attempting to preserve the stalk is time-consuming and sometimes demanding, but it is rewarded with improved endocrinological results.

In a case series reported by Honegger et al., endocrine function in relation to pituitary preservation in patients undergoing transcranial surgery showed diabetes insipidus in 62% of patients, adrenal failure in 58% of patients, and hypothyroidism in 32% of patients. Endocrinological results associated with pituitary preservation in patients undergoing transsphenoidal surgery demonstrated diabetes insipidus in 90.9% of patients, adrenal failure in 63.6% of patients, and hypothyroidism in 72.7% of patients. In our series, pituitary function was not preserved in any of the patients who underwent stalk transection. Of the 24 patients with stalk preservation, 58.3% received total HRT. However, 8.3% of the patients received partial HRT, and intact pituitary function was observed in 33.4% of the patients. The pituitary stalk and gland are worth preserving during surgery because the preservation of these structures increases the likelihood of maintaining intact anterior pituitary functions.

Honegger et al. reported that, in general, the results of endocrinological testing at 3 months after surgery predicted the final endocrine outcome, but some patients may have delayed pituitary dysfunction and others might improve during later follow-up evaluations. In our case series, we checked patients’ endocrine function preoperatively and 2 weeks postoperatively; in view of the possibility of delayed changes, the timing of our evaluation of endocrine function represents a limitation of our study.

It has been reported in the literature that the degree of postoperative endocrinological deficiency depends on the extent of tumor removal. Other authors have suggested that endocrine function is only at risk if the solid tumor and capsule are dissected from structures that regulate this function. In our series, the endocrinological findings were similar regardless of whether complete removal was accomplished. Of the 18 patients who underwent total tumor removal and stalk preservation, 33.3% showed intact pituitary function and 5.6% received partial HRT. Of the 6 patients in whom subtotal or partial removal was performed and the stalk was preserved, 16.7% received partial HRT and 33.3% had intact pituitary function. Therefore, the factor determining complete or incomplete
tumor removal had no influence on endocrinological outcome in our series.

Recurrence Rates Associated With Pituitary Stalk Preservation

The general consensus is that the best results of surgery for craniopharyngioma occur after the complete excision of the tumor, which should be the goal of primary intervention.6,10,13 Recurrence rates dramatically increase if craniopharyngiomas are incompletely removed, and subsequent operations can prove even more difficult. In our 39 patients (excluding the 2 who received radiotherapy), the overall recurrence and regrowth rate was 25.6%, and there was a statistically significant difference in recurrence-free survival between patients in whom complete tumor resection was accomplished and those in whom tumor resection was incomplete.

We assessed the relationship between tumor recurrence and pituitary stalk preservation because craniopharyngiomas often originate from the pituitary stalk. In our series, the recurrence rate was 23.3% (7 of 30) in patients in whom the stalk was preserved and 33.3% (3 of 9) in patients in whom stalk section was performed. There was no statistically significant association between stalk preservation and increased recurrence rates.

Management Philosophy

The surgical management of craniopharyngiomas remains challenging; however, many improvements have been made in the treatment of these lesions, including HRT, the surgeon’s ability to choose ideal surgical approaches on the basis of MR imaging studies, and microsurgical mastery of the anatomy. The newly defined goal of total tumor excision has been achieved within the past decade.17,21,25 As stated by Van Effenterre and Boch,22 the goal of craniopharyngioma surgery should be “complete removal with improved visual function, minimal deterioration of endocrine function, and no neuropsychological impairment.” Nevertheless, attempts to radically excise the tumor have rendered significant morbidity by causing injury to the hypothalamus, vasculature, endocrine system, or optic apparatus. The goal of surgery is excision of as much of the tumor as possible, without incurring neurological or neuropsychological complications, so that the patient can maintain a good quality of life. It is easier to accept a subtotal resection than a serious complication.

Although endocrine loss can be overcome by using HRT, such treatment is associated with several complications.4,14 Steroid replacement therapy typically consists of the administration of cortisol. Prednisone and hydrocortisone are the most commonly prescribed oral preparations of cortisol. The dosage may need to be temporarily increased during periods when the body is stressed due to illness, infection, surgery, or trauma. Thyroid HRT usually includes the administration of thyroxine. Blood levels are closely monitored as over-replacement may cause complications, such as osteoporosis or heart disease. Antidiuretic hormone is currently replaced by the administration of desmopressin acetate, a synthetic version of the hormone, administered in the form of a pill, nasal spray, or injection. Vasopressin deficiency causes diabetes insipidus, with excessive thirst and urination. Patients may become severely dehydrated if they do not drink enough liquid. We assessed our patients’ endocrinological features after surgery for craniopharyngioma, the differences in the anatomical and functional preservation of the pituitary gland, and the relationship between with tumor recurrence and pituitary stalk preservation, with a special focus on endocrinological outcomes.

Visual Outcome

The first sign of craniopharyngioma is usually the development of progressive visual field defects, which will result in permanent vision loss unless the tumor is removed. Preoperatively, 65.2% of the patients in this case series presented with visual loss, and this fact attests to the preponderance of the suprasellar mass in this
showed no change in vision. In our study, 50% of the patients showed improvement after surgery, 33.3% showed visual deterioration, and 16.7% showed no change in vision.

Conclusions

Despite stalk preservation at surgery, the percentage of patients with normal hormone function was 33.4%, and 8.3% of patients received partial HRT. Nevertheless, the pituitary stalk must be preserved whenever possible with maximal tumor resection to increase the chance that intact anterior pituitary functions can be maintained. The results of the present study show that pituitary stalk preservation may not be related to increased recurrence rates.

Disclosure

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