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Long-term neurological, visual, and endocrine outcomes following transnasal resection of craniopharyngioma

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Object. The authors report on a cohort of patients with craniopharyngioma treated principally through transnasal (TN) resection and followed up for a minimum of 5 years. More specifically, they evaluate the role of the TN approach in the management of craniopharyngioma.

Methods. Between 1984 and 1994, 68 patients underwent TN resection of craniopharyngiomas at the University of Southern California. The tumor was at least partially cystic in 88% of cases. Four tumors were purely intrasellar, 53 had intra- and suprasellar components, and 11 were exclusively suprasellar. During the same period, 18 patients underwent transcranial (TC) resection of purely suprasellar craniopharyngiomas. Long-term neurological, visual, and endocrine outcomes were reviewed for all patients.

In 61 (90%) of 68 patients in the TN group, total resection was achieved, according to 3-month postoperative magnetic resonance images, although four patients suffered a recurrence. Three (43%) of the seven tumors that had been partially resected were enlarged on serial imaging. Fifty-four (87%) of 62 patients with preoperative visual loss experienced improvement in one or both eyes, but two patients (3%) with exclusively suprasellar tumors experienced postoperative visual worsening in one or both eyes. New instances of postoperative endocrinopathy (that is, not present preoperatively) occurred as follows: hypogonadism (eight of 22 cases), growth hormone (GH) deficiency (four of 18 cases), hypothyroidism (11 of 49 cases), hypocortisolemia (nine of 52 cases), and diabetes insipidus (DI; four of 61 cases). One case each of hypocortisolemia and hypothyroidism resolved after surgery. Hyperphagia occurred in 27 (40%) of 68 patients. One patient had short-term memory loss. Postoperative complications included one case of cerebrospinal fluid leak.

Among the 18 patients in the TC group, 11 had complete resections. In one case (9%) the tumors recurred. Three (43%) of the seven subtotally resected tumors grew during the follow-up interval. Vision improved in 11 (61%) of 18 cases and worsened in three (17%) as a result of surgery. New instances of postoperative endocrinopathy occurred as follows: hypogonadism (one of six cases), GH deficiency (four of seven cases), hypothyroidism (11 of 14 cases), hypocortisolemia (eight of 15 cases), and DI (nine of 16 cases). No instance of preoperative endocrinopathy was corrected through TC surgery. Four patients (22%) exhibited short-term memory loss and 11 (61%) had hyperphagia after surgery. When compared with those in the TC group, patients in the TN group had shorter hospital stays.

Conclusions. Use of the TN approach can render good outcomes in properly selected patients with craniopharyngioma, particularly when the tumor is cystic. Even in mostly suprasellar cases, an extended TN approach can afford complete resection. Note that endocrine function often worsens after surgery and that postoperative obesity can be a significant problem.

Key Words • craniopharyngioma • long-term outcome • endocrine outcome • extended transsphenoidal approach

Craniopharyngioma is a rare tumor having a calculated incidence of 338 cases per year in the US, with one third occurring in children younger than 14 years of age.[3] Although histologically benign, the lesion's potential for adhesion to vital brain structures makes total resection, and thus cure, difficult. The challenges presented by this tumor have been well documented.[2,4,6,11,16,24,25,34,37,39,42,45] Removal of the tumor at the expense of pituitary function has become clinically tolerable with the development of hormonal replacement therapy.[17] Nonetheless, surgical cure that results in hypothalamic or optic injury can be unacceptable.

Neurosurgeons currently disagree on the optimal management of craniopharyngiomas. Although some advocate complete tumor removal,[12,40,45] others favor limited resection followed by radiotherapy.[2,11,25] Surgical removal of the tumor can be accomplished through a variety of corridors including TC (pterional, subfrontal, subtemporal, and bifrontal–interhemispheric) or TN routes.[16,27,32,45] In this study, we aimed to elucidate the current role of TN surgery for craniopharyngioma in an era of sophisticated microsurgery and advancing radiosurgery.

Although there is consensus that purely intrasellar craniopharyngiomas should be removed via the TN approach, these tumors are rare. No such consensus exists for craniopharyngiomas that are suprasellar or have significant suprasellar extension. The TN approach has advantages over other routes, including a reduced postoperative hospital stay.[12,21,24,27] The possibility of incomplete resection, how-

Abbreviations used in this paper: βHCG = beta human chorionic gonadotropin; CSF = cerebrospinal fluid; DI = diabetes insipidus; GH = growth hormone; MR = magnetic resonance; TC = transcranial; TN = transnasal.

ever, as well as the risk of CSF leaks has generated concerns about the TN approach. We report on a series of 86 patients with craniopharyngiomas; a TN approach was used in 68 patients and a TC route was followed in 18. Although some investigators have examined the TN approach for craniopharyngioma,[26] rigorous pre- and postoperative endocrine data have not been previously reported in the neurosurgical literature. The use of the extended TN approach for suprasellar tumors is also discussed.

Clinical Material and Methods

Patient Population

Between 1984 and 1994, 86 patients underwent surgical treatment for craniopharyngioma (M.H.W.). These dates were selected to limit the study to patients with at least 5 years of follow up and those who had undergone MR imaging. In each case, the operation was the exclusive procedure performed in the patient; that is, none of the patients had prior or repeated surgery. All tumors were histologically confirmed through permanent staining of intraoperatively obtained tissue sections. Cases with questionable or mixed pathology were not included in this series.

We retrospectively reviewed the hospital charts and imaging studies for each of the patients. All research was conducted in accordance with local institutional review board policies. The patients were grouped according to surgical approach (TN compared with TC) and analyzed for surgical data, endocrine and visual outcomes, long-term morbidity and mortality rates, and recurrence rates.

The TN group comprised 68 patients (35 female and 33 male) ranging in age from 30 months to 73 years. The 18 patients (10 men and eight women) included in the TC group had ages rangning from 22 to 76 years. The TN route was selected in all cases in which the tumor was purely intrasellar (four cases), intrasellar with suprasellar extension and predominantly cystic (53 cases), or purely suprasellar and cystic (11 cases; Table 1). Altogether 60 (88%) of 68 patients in the TN group harbored at least partially cystic lesions. The eight solid lesions were intrasellar tumors, four having a small suprasellar extension. The TC method was chosen when the lesion's suprasellar component was preponderant and solid or lateral to the midline.

Outcome Assessment

Patients were examined (M.H.W.) preoperatively, at 3 months, and at regular intervals thereafter. Additionally, an ophthalmologist evaluated the patients at these times. The duration of follow up ranged from 5 to 10 years.

Patients were also treated by endocrinologists. Complete serum endocrine panels were obtained preoperatively and at 3 months postoperatively. Provocative endocrine testing was not performed. Gonadotropin (follicle-stimulating hormone and luteinizing hormone), fasting GH, insulin-like growth factor, thyroid-stimulating hormone (T3 and T4), fasting morning and 4:00 p.m. cortisol, and prolactin levels were tested in all patients except 10 from the TN group and four from the TC group who lacked preoperative GH testing. Diabetes insipidus was diagnosed clinically by using urine specific gravity and serum sodium levels. Cerebrospinal fluid was withdrawn from five patients with suprasellar solid lesions supposed to be germ cell tumors to look for βHCG. All five of these cases were in the TC cohort.

TABLE 1

Tumor characteristics in 86 patients

Tumor Component	TN Group (%)	TC Group (%)
total no. of tumors	68	18
intrasellar	4 (6)	0 (0)
intra- & suprasellar	53 (78)	0 (0)
suprasellar	11 (16)	18 (100)
cystic & solid	60 (88)	8 (44)
solid	8 (12)	10 (56)

Surgical reports, anesthesia records, and nursing notes were analyzed for intra- and perioperative data. Information regarding surgical time, blood loss, duration of hospital stay, use of transfusion products, and use of graft for closure of CSF leaks was also cataloged. Follow up of global outcomes were recorded in categorical terms. A patient was classified as having a "good outcome" if he or she was able to return to baseline levels of professional and social function and did not have neurological deficits, as assessed by the patient, physician, and family. Many of these patients required pituitary replacement therapy, which did not interfere with participation in activities of daily living. Patients with some neurological debility and only mildly impaired activities of daily living were categorized as having "fair outcomes." All other outcomes were classified as "poor."

Radiographic Assessment

Radiographic evaluation was performed using preoperative MR imaging in all cases. In addition, most patients also had computerized tomography scans and plain skull x-ray films available for preoperative planning, especially in the TN cases. Postoperatively, we used only MR imaging with high-resolution, thin-sectioned enhanced views of the sellar and parasellar areas. We did not use computerized tomography postoperatively because neuroradiologists at our facility believe the MR imaging studies are sensitive and sufficient. All images were reviewed by staff neuroradiologists and the senior author (M.H.W.). Tumors were evaluated for size, diameter, and sprawl above and below the diaphragma sellae. All patients underwent MR imaging at 3 months postoperatively. Furthermore, MR imaging was repeated whenever signs or symptoms indicated recurrence or tumor growth.

Of the tumors accessed transnasally, 60 (88%) had mixed solid and cystic components; the remaining eight (12%) were solid (Table 1). The transcranially approached tumors were mixed solid and cystic in eight cases (44%), and the remaining 10 cases (56%) were solid.

Although no sign of increased intracranial pressure was seen on presentation, two (3%) of the 68 patients in the TN and four (22%) of the 18 patients in the TC group demonstrated hydrocephalus radiographically.

Surgical Approaches

Details of the TN approach have been published previously.[43] In cases in which the tumor was purely intrasellar, the standard route was used and only the floor of the sella turcica was removed. For tumors with suprasellar extension, however, the extended TN approach was undertaken.

TABLE 2

Preoperative findings in 86 patients harboring craniopharyngioma

Variable	TN Group (%)	TC Group (%)
total no. of patients	68	18
visual loss	62/68 (91)	18/18 (100)
endocrinopathy		
GH deficiency	40/58 (69)	7/14 (50)
hypogonadism	30/52 (58)	12/18 (67)
hypothyroidism	19/68 (28)	4/18 (22)
hypoadrenalism	16/68 (24)	3/18 (17)
DI7/68 (10)	2/18 (11)	

TABLE 3

Endocrinological function in 86 patients following resection of craniopharyngioma

Variable	TN Group (%)	TC Group (%)
hypogonadism	38/52 (73)	13/18 (72)
improved cases	0/30 (0)	0/12 (0)
new cases	8/22 (36)	1/6 (17)
hypothyroidism	30/68 (44)	15/18 (83)
resolved cases	1/19 (5)	0/4 (0)
new cases	11/49 (22)	11/14 (79)
hypocortisolemia	25/68 (37)	11/18 (61)
resolved cases	1/16 (6)	0/3 (0)
new cases	9/52 (17)	8/15 (53)
DI	48/68 (71)	11/18 (61)
resolved cases	0/7 (0)	0/2 (0)
new cases	41/61 (67)	9/16 (56)
GH deficiency	44/68 (65)	11/18 (61)
resolved cases	0/40 (0)	0/7 (0)
new cases	4/18 (22)	4/7 (57)

In this extended procedure, bone removal continued across the tuberculum toward the planum sphenoidale, thus affording access to the suprasellar cistern. In cases in which the arachnoid had been violated, an abdominal fat graft or tensor fascia lata graft was applied to seal the opening in the sellar floor and the sphenoid sinus was packed with fat.

During all TC operations, a standard pterional craniotomy was performed followed by subfrontal or transsylvian dissection as required. No case was treated using combined approaches.

Radiotherapeutic Treatment

All patients who had undergone subtotal resections—as demonstrated during surgery or on follow-up imaging—were referred for external-beam radiotherapy. Patients received 4800 to 5000 cGy radiation fractionated over 5 weeks.

Results

Clinical Presentation

Eighty (93%) of the 86 patients in this series had presented with visual compromise that was confirmed on formal evaluation of visual fields (Table 2). This group consisted of 62 (91%) of 68 patients who had undergone the TN procedure and all 18 patients in the TC group. The other six patients (7%) had presented with symptoms attributable to hypopituitarism and included the four patients with purely intrasellar tumors and two of the patients with combined intra- and suprasellar tumors. Of the 80 patients who had presented with visual loss, 63 (79%) demonstrated some form of asymptomatic hypopituitarism on formal testing.

Growth hormone levels were measured in 72 patients, and GH deficiency was demonstrated in 40 (69%) of 58 and seven (50%) of 14 patients in the TN and TC groups, respectively (Table 2). Gonadotrope function could not be measured in 16 patients in the TN group because they were too young; of the remaining 52 patients, however, 30 (58%) were hypogonadal. Twelve patients (67%) in the TC group were hypogonadal. Hypothyroidism was noted in 19 (30%) of 68 and four (22%) of 18 patients in the TN and TC groups, respectively. Hypocortisolemia was demonstrated in 16 patients (24%) in the TN group and three (17%) in the TC group. Diabetes insipidus was noted in seven patients (10%) from the TN group and two (11%) in the TC group.

Endocrine Outcome

Postoperative endocrine data were tabulated and compared (Table 3). Four new cases of GH deficiency occurred in both groups of patients; therefore, the postoperative rate of GH deficiency was 65 and 61% in the TN and TC cohorts, respectively. None of the preoperative cases of deficiency resolved after surgery.

Among patients in the TN group who had demonstrated no preoperative hypogonadism, eight (36%) of 22 had hypogonadism postoperatively. Inadequate gonadal function also occurred in one (17%) of six of the patients in the TC group who had revealed no preoperative evidence of the disease. Thus, the postoperative incidences of hypogonadism were 73 and 72% in the TN and TC cohorts, respectively. Hypogonadism did not improve in the patients who had presented with the disease preoperatively.

New cases of hypothyroidism were discovered in 11 of the 49 patients (22%) in the TN group who had not demonstrated the disease preoperatively, resulting in a postoperative incidence of 44%. In this cohort, only one (5%) of 19 patients with preoperative hypothyroidism experienced resolution of this problem. Eleven (79%) of 14 patients in the TC group suffered new cases of hypothyroidism, and none of the four with preoperative hypothyroidism improved. Thus, 83% of the TC cohort displayed hypothyroidism postoperatively.

In the TN group, one (6%) of 16 cases of hypocortisolemia resolved. Unfortunately, nine (17%) of 52 patients acquired this insufficiency after surgery. The TC cohort had eight (53%) of 15 new cases, with no evidence of any improvement among the three who had been hypocortisolemic prior to surgery. The postoperative rate of hypocortisolemia was 37 and 61% in the TN and TC groups, respectively.

Diabetes insipidus was the most common iatrogenic endocrinopathy in both cohorts. It postoperatively occurred in 41 (67%) of 61 patients in the TN group and nine (56%) of 16 in the TC cohort. Preoperative cases of DI did not improve with surgery in either group. Thus, the postoperative incidences of DI were 71 and 61% in the TN and TC groups, respectively.

In the five cases of suspected germ cell tumors in the TC cohort, preoperative βHCG levels ranged from 8 to 26 mIU/L.

TABLE 4

Visual outcome in 86 patients following resection of craniopharyngioma

Vision Status	TN Group (%)	TC Group (%)
improved	54/62 (87)	11/18 (61)
unchanged	12/68 (18)	4/18 (22)
worsened	2/68 (3)	3/18 (17)

TABLE 5

Complications following resection of craniopharyngioma in 86 patients

Variable	TN Group (%)	TC Group (%)
total no. of patients	68	18
CSF leak	1 (1)	0 (0)
meningitis	0 (0)	1 (5)
short-term memory loss	1 (1)	4 (22)
hyperphagia	27 (40)	11 (61)

Functional Outcome

Common experiences in both groups of patients were hyperphagia and weight gain. In particular, they occurred in 27 (40%) of 68 patients in the TN group. Hyperphagia was also seen in 11 (61%) of 18 cases in the TC group. Postoperative obesity remained a significant problem in these patients.

Short-term memory loss occurred in one (1.5%) of 68 in the TN group and four (22%) of 18 in the TC group. This deficit remained stable on long-term follow up.

No patient died during the follow-up period, and no alteration of consciousness occurred in either cohort. Ninety-four percent of the patients in this series had good outcomes, including 67 (99%) of 68 in the TN group and 14 (78%) of 18 in the TC group. All of these patients resumed preoperative levels of social and professional activity. The five patients with memory loss were unable to resume their preoperative professional status and were thus assessed as having a fair outcome. No patient was assessed as having a poor outcome.

Hydrocephalus Outcome

Neither of the two patients with ventriculomegaly in the TN group had signs of hindered CSF circulation postoperatively. Follow-up MR images demonstrated resolution, and the patients did not require placement of a shunt. Two of the four patients with ventriculomegaly in the TC group had clinically and radiographically apparent hydrocephalus following surgery and required a second procedure for shunt placement.

Visual Outcome

On postoperative evaluation, two (3%) of 68 patients who had undergone TN procedures experienced worsening of their preoperative visual loss, including one patient with binocular deterioration (Table 4). Both of these patients had exclusively suprasellar tumors. Visual symptoms were ameliorated in 54 (87%) of 62 patients with preoperative visual impairment. The other 12 patients in the TN group had no change in vision, including all six patients who had presented with hypopituitarism. Among the patients in the TC group, three (17%) of 18 suffered worsening of vision, including two with binocular deterioration. Eleven (61%) of 18 did have some improvement of vision following removal of the tumor via the TC approach. No person was rendered blind in any eye.

Perioperative Data

The surgical time ranged from 53 to 105 minutes in the TN group and from 222 to 308 minutes in the TC group. Blood loss in the TN cohort was 30 to 180 ml, whereas it was 160 to 350 ml in the TC group. No patient in either group required a blood transfusion. The mean duration of the hospital stay was 4.2 and 7.8 days in the TN and TC groups, respectively. Intraoperative repair of CSF leaks (graft for closure) in the TN group was required in 58 (85%) of 68 cases.

Perioperative Complications

In the TN group, only one case of CSF leak occurred postoperatively (Table 5). This leak was successfully treated during a second procedure, that is, endoscopically guided sinus packing with autologous fat. No case of meningitis occurred. No CSF leak was noted in the TC group, but there was one case of meningitis (one [6%] of 18). This disease was treated using antibiotic agents alone without further sequelae.

Recurrence Rates

Total resection was confirmed on 3-month postoperative MR imaging in the TN group in 61 cases (90%). Of the seven patients (10%) in the TN group who had undergone subtotal resections, five subsequently received conventional fractionated radiotherapy. Among the 61 patients in the TN group who had demonstrated total resection on 3-month postoperative imaging studies, we counted four recurrences (7%) based on MR images obtained during the 5- to 10-year follow ups. Three (43%) of seven subtotally resected cases in the TN group had progressive tumor enlargement on serial imaging, including two patients who had not received radiotherapy. These numbers yield a total recurrence rate of 10% (seven of 68 cases).

Among the cohort who underwent the TC approach, total resection was confirmed on 3-month postoperative MR imaging in 11 cases (61%). Six of the seven subtotally resected tumors were treated with adjuvant conventional radiotherapy, as mentioned earlier. On the 5- to 10-year follow-up imaging studies, recurrence was noted in one (9%) of 11 totally resected lesions and progressive enlargement in three (43%) of seven subtotally removed tumors including two not previously radiated. Therefore, four (22%) of 18 patients treated via the TC approach experienced recurrences.

Discussion

Management Philosophy

As stated by Van Effenterre and Boch,[40] the goal of craniopharyngioma surgery should be "complete removal with improved visual function, minimal deterioration of endocrine function, and no neuropsychological impairment." Clearly, radical resection that results in impaired memory or level of consciousness cannot be considered acceptable.

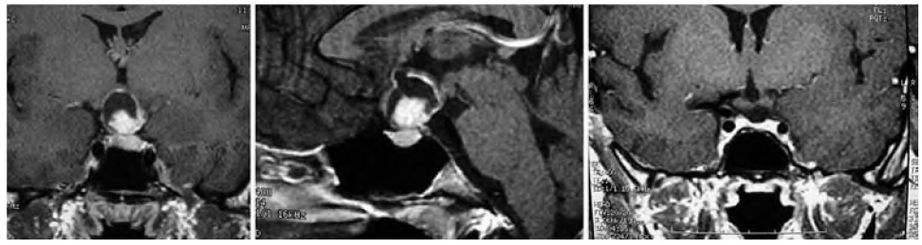

FIG. 1. Coronal *(left)* and axial *(center)* T_1-weighted postcontrast MR images obtained preoperatively, demonstrating a suprasellar craniopharyngioma with nodular and cystic portions. The tumor was approached via an extended transsphenoidal route. A coronal MR image *(right)* obtained 4 years after surgery, revealing complete resection.

Note, however, that endocrine loss can be overcome by using hormonal replacement therapy, thus allowing the surgeon to be more aggressive. Much less forgiving is injury to the hypothalamus, vasculature, or optic apparatus. A subtotal resection, especially in young patients, almost always requires further surgery or radiotherapy with a decreased chance of complete tumor removal compared with that on the initial encounter. The goal for the surgeon, in our opinion, is the removal of as much tumor as possible during the initial operation while leaving the rest for control with radiosurgery. Maintaining a good quality of life is the precept. It is easier to accept a subtotal resection than a serious complication.

Attempts to radically excise have rendered significant morbidity, although the procedure has its proponents.[4,16,34,37,39,45] In a review of 144 cases treated through surgery in which the goal was total removal in every case, 90% had complete resections.[45] Of these totally resected cases, 67.4% had good clinical outcomes, whereas there was a 16.7% mortality rate and a 16% morbidity rate. Authors of another large surgical series with a more conservative surgical outlook reported 59% total and 29% subtotal resections.[40] Note, however, that 13 and 33%, respectively, of the cases in these two groups recurred and most were treated with repeated surgery. No patient was referred for radiotherapy. On long-term neuropsychological testing, 91% had normal social integration. An even more conservative approach was taken in another surgical series in which the authors achieved complete resection in only seven (9.5%) of 74 cases.[2] Nonetheless, long-term follow-up data revealed that more than 90% of the patients experienced disease remission. In this series, subtotal resection plus radiotherapy yielded excellent results. Although microneurosurgery has advanced along with imaging guidance, the risk of significant morbidity remains if radical resection is the exclusive goal in each case.

Aggressive surgical management may not lead to optimal outcomes, and the current literature favors a limited surgical approach followed by radiotherapy.[2,6,11] The role of radiotherapy in controlling tumor while maintaining good function of surrounding critical structures is well recognized, and craniopharyngiomas are generally considered radiosensitive. Progression-free survival is improved significantly if radiotherapy is added to the treatment regimen postoperatively.[7,11,13,19,28,35,38,41,44] Although long-term data are not available, the use of stereotactic radiosurgery has shown promising tumor control as well.[5,20,30] With its known benefits and few side effects, radiation in conjunction with limited surgery in cases in which tumor is adhesive to critical structures offers the best chance of controlling tumor and maintaining baseline quality of life. Additionally, the use of fractionated radiotherapy may further improve the ability to apply radiation near critical optic apparatus.[41]

Selection of the best management for craniopharyngioma ultimately depends on each patient's age and medical condition, surgeon and patient preference, experience of the surgeon, and postoperative radiotherapy options available. One must recognize that advances in stereotactic radiosurgery alter traditional surgical paradigms. Resection via the TN route is a good option for performing a less morbid surgical procedure while allowing for the possibility of radical resection in appropriately selected cases. With cystic tumors, the TN approach can limit surgical morbidity and provide a good chance for complete resection.

Selection of Surgical Approach

Others have previously described their experience with the TN approach for craniopharyngioma.[1,12,18,21,22,24,25,27] Authors of another recent publication revisited the role of transsphenoidal surgery but did not include rigorous endocrine data.[26] In 1932 Cushing[9] was the first to use this approach for craniopharyngioma. Later, in 1963, Hardy and Lalonde[14] repopularized the procedure. Since then, however, the TC approaches have been preferred in most cases except solely intrasellar lesions (Fig. 1).

The discussion of which approach is appropriate often hinges on whether the tumor origin is above or below the diaphragma sellae. Most authors agree that the TN approach should be used in those cases in which the mass causes expansion of the sella. It is believed that this circumstance assures a tumor origin below the diaphragm and a good chance for total removal.[6,18,25,27] Tumors below the diaphragm may remain intrasellar, causing expansion of the diaphragm, or may grow above the diaphragm, forming a dumbbell-shaped lesion. These locations are amenable to TN approaches because expansion of the diaphragm, which acts as a barrier to pial invasion, facilitates complete resection.

We acknowledge a referral bias in the cases in this series, as sellar pathology is an area of expertise for the senior author. This fact may have affected the location of the tumors treated at our institution, as the majority of the tumors (57 [66%] of 86) did have intrasellar involvement. In most reports, intrasellar involvement occurs in approximately one third of the cases.[21,27] In the TN cohort, however, there were only four cases of purely intrasellar craniopharyngioma, 53 with an intrasellar component also had significant suprasellar extension, and 11 were purely suprasellar. We believe

these results support the use of the TN approach for primary treatment of craniopharyngioma, even in cases in which the tumor has a significant suprasellar presence, as recently reported by Maira, et al.[26]

Selection criteria for a particular approach in this series depended on whether the tumor was cystic. In cases in which the tumor was largely cystic or the majority of the solid portion was intrasellar, the lesion was removed via the TN approach. Therefore, suprasellar cystic tumors were accessed transnasally. Suprasellar solid tumors, however, were treated via the TC approach. During the TN approach, suprasellar cystic lesions are punctured and internally decompressed. Then the tumor capsule can be gently teased from surrounding structures and, in many cases, removed en bloc. In purely suprasellar cystic tumors, an extended TN approach is used. Clearly, surgeon comfort and experience are crucial in using this approach, but radical removal is possible and is justified by our experience, as we have completed total excision in many cases of suprasellar extension. This feat is not without risk, however, and considerable facility with the procedure is required.[6]

Others have noted that significant intracranial extension does not necessarily preclude the TN approach as long as the tumor is cystic and calcification—an indication of tumor adhesiveness—is not significant.[18,24] In these cases, palliation can be achieved; however, these authors believe that total resection is unlikely in this scenario. Some assert that regardless of suprasellar extension, a TN approach should be used if any portion of the tumor is intrasellar, because it is less traumatic to the patient.[27]

The aim of our study was to analyze endocrine and clinical outcomes in a series of patients harboring craniopharyngioma that were treated mainly via the TN approach. In other series in which any cases were treated transnasally, the outcomes in comparison with those of the TC groups were always better.[11,12,27] In fact, significantly lower recurrence rates following subtotal resections of primarily intrasellar tumors have been reported.[11,22] These findings reflect the extrapial location of tumor as well as a smaller lesion size in cases selected for TN resection. As in our experience, others have noted that intra- and suprasellar tumors are more often cystic and soft, whereas suprasellar tumors are solid.[26]

Irregularly shaped suprasellar tumors are difficult to resect as they extend beneath the pia mater and have higher recurrence rates.[27] These cases are most often approached transcranially, and thus it is difficult to compare outcomes directly between TC and TN surgical groups. Note, however, that duration of hospital stay, operating time, and blood loss were significantly lower in our TN cohort, corroborating the assumption that the TN approach is less invasive to the patient.

Recurrence Rates

The long-term outcomes in this series are acceptable and consistent with those in other reports in the literature.[1,12,18,21,22,24,26,27] The general consensus is that the best results with craniopharyngioma occur after complete excision of the tumor, which should be the goal of the primary intervention.[1,6,12,18,21,22,24,25,27] Subtotal or partial resections create conditions for recurrences, and repeated operations can prove even more difficult. Within this series, the TN approach did not limit our ability to achieve total resection.

The majority of relapses occur within the first 3 years after surgery.[12,18,40] The minimal follow up in the present series was 5 years, with many patients followed up for 10 years. Four (6.5%) of the 61 totally resected tumors in the TN group recurred and three (43%) of the seven subtotally resected tumors enlarged. In other TN series reported, the rates between these two resection groups ranged from 0 to 13% and 24 to 60%, respectively.[1,12,18,21,22,24,25,27] Transcranial totally resected craniopharyngioma operations generally yield recurrence rates from 7 to 13%.[2,27,40,45] Among the subtotally resected cases, tumor growth occurred in 10 to 33%. The TC cohort in the present series had a 22% combined regrowth and recurrence rate.

Visual Outcome

Most patients (80 of 86) in this series presented with visual loss. This fact attests to the preponderance of the suprasellar mass in this series. Rapid decompression of visual apparatus is one advantage of the TN approach. Vision improved in 87% of cases; however, it deteriorated in two cases in the TN group and in three cases in the TC group. In each of these cases, the tumors were exclusively suprasellar. Visual improvement after TN surgery has been noted in 70 to 94% of patients.[12,21,40] In the present study, visual outcomes were worse in the TC cases. This finding likely is related to the fact that suprasellar solid tumors are more adhesive to surrounding neural structures.

Endocrine Outcome

The TN approach likely leads to endocrinopathy, although to what extent has yet to be clearly documented. On the other hand, the endocrine outcome in largely TC series has been reported.[17] To our knowledge, this is the only report with detailed endocrine outcomes in a largely TN series for craniopharyngioma. Almost no preoperative endocrinopathy improved after surgery. In fact, new postoperative endocrine abnormality should be expected following surgery for craniopharyngioma.[12,18] Some assert that the use of the TN approach is more appropriate in patients with hypopituitarism because of the high rate of postoperative endocrinopathy.[24]

In the TN cohort, all categories of endocrinopathy were more common after surgery. The greatest increase was in the incidence of DI, which rose from 10 to 71%. Increases in DI have been well documented; however, in previous TN series, they have ranged from 11 to 30%.[17,25,27] The rates in the present study were higher and correlated more with those documented in mainly TC series in which radical resection was the goal.[40,45] Other endocrine axes are not as well studied in the literature. In the TN cohort reported on here, changes in the other endocrine axes after surgery were less dramatic, although rates were generally higher on presentation compared with those in the TC group. The patients treated via the TC approach had more profound deterioration of endocrine function but presented with lower rates of deficiency; for example, hypothyroidism increased from 22.2 to 83.3%, DI from 11 to 61%, and hypocortisolemia from 17 to 61%.

In one study, resolution of an endocrine dysfunction occurred in 19% of patients.[21] This result was not reproduced in our experience. The reversal of endocrinopathy is rare. Hyperprolactinemia seems to be the most likely deficiency

to improve, with eight of 16, three of three, and three of four cases improving in three separate series.[17,25,27] Hypogonadism and GH secretion also have been shown to improve.[17,27]

Cerebrospinal fluid βHCG levels of 8 to 28 mIU/L were demonstrated in five cases of suprasellar solid lesions; however, surgical pathology results confirmed craniopharyngioma. Raised βHCG levels in the context of craniopharyngioma have been reported.[15] Its presence in the CSF may indicate leakage of tumor contents.

Postoperative Hyperphagia

Hyperphagia was a postoperative occurrence that led to morbidity in a considerable number of patients: 40% (27 of 68) and 61% (11 of 18) of patients in the TN and TC groups, respectively. Hyperphagia and postoperative obesity are well-recognized complications in surgery for craniopharyngioma,[8,11,23,33,36] although both are mainly discussed in the nonsurgical literature. Authors of most surgical series do not discuss their presence or absence. Data from one large series demonstrated that both were very infrequent;[12] in another, however, both occurred 35% of the time.[11]

The origin of hyperphagia involves damage to the satiety center in the ventromedian hypothalamus.[11,31] Results of pathological studies have shown the propensity for craniopharyngioma to create finger-like projections within brain parenchyma, and these projections may lead to hypothalamic injury when the tumor capsule is removed.[29] In one study, authors used MR imaging confirmation of hypothalamic damage in children with postoperative obesity following resection of craniopharyngioma.[10] In some patients, psychosocial difficulties occur and can be overwhelming to family members, with rehabilitation proving very difficult.[33] Little is written about this unfortunate complication.

Despite the relative ease of tumor dissection in most cases in the present study, hypothalamic injury did occur in some. This result should serve as a warning to exercise caution while performing a dissection near the hypothalamus and sharply amputate the tumor capsule in this area. Postoperative obesity reported in this series likely represents the true incidence of this complication of craniopharyngioma removal. Future investigators should focus more on its ramifications and neuropsychological outcomes.

Conclusions

For cystic craniopharyngioma along the hypothalamopituitary axis, the TN approach provided a less invasive method with good outcome. Suprasellar solid tumors fared worse with regard to endocrine, visual, and hypothalamic injury. Postoperative obesity is a significant problem. For the goal of palliation, the role of the TN approach is clear. In a surprising number of cases, however, radical resection was also possible by using an extended TN route.

References

1. Abe T, Ludecke DK: Transnasal surgery for infradiaphragmatic craniopharyngiomas in pediatric patients. **Neurosurgery 44:** 957–966, 1999
2. Baskin DS, Wilson CB: Surgical management of craniopharyngiomas. A review of 74 cases. **J Neurosurg 65:**22–27, 1986
3. Bunin GR, Surawicz TS, Witman PA, Preston-Martin S, Davis F, Bruner JM: The descriptive epidemiology of craniopharyngioma. **J Neurosurg 89:**547–551, 1998
4. Carmel PW, Antunes JL, Chang CH: Craniopharyngiomas in children. **Neurosurgery 11:**382–389, 1982
5. Chung WY, Pan DH, Shiau CY, Guo WY, Wang LW: Gamma knife radiosurgery for craniopharyngiomas. **J Neurosurg 93 (Suppl 3):**47–56, 2000
6. Ciric IS, Cozzens JW: Craniopharyngiomas: transsphenoidal method of approach—for the virtuoso only? **Clin Neurosurg 27:** 169–187, 1980
7. Crotty TB, Scheithauer BW, Young WF Jr, Davis DH, Shaw EG, Miller GM, et al: Papillary craniopharyngioma: a clinicopathological study of 48 cases. **J Neurosurg 83:**206–214, 1995
8. Curtis J, Daneman D, Hoffman HJ, Ehrlich RM: The endocrine outcome after surgical removal of craniopharyngiomas. **Pediatr Neurosurg 21 (Suppl 1):**24–27, 1994
9. Cushing H: **Intracranial Tumours: Notes Upon a Series of Two Thousand Verified Cases with Surgical-Mortality Percentages Pertaining Thereto.** Springfield, IL: Charles C Thomas, 1932, pp 93–98
10. de Vile CJ, Grant DB, Hayward RD, Kendall BE, Neville BG, Stanhope R: Obesity in childhood craniopharyngioma: relation to post-operative hypothalamic damage shown by magnetic resonance imaging. **J Clin Endocrinol Metab 81:**2734–2737, 1996
11. Duff JM, Meyer FB, Ilstrup DM, Laws ER Jr, Schleck CD, Scheithauer BW, et al: Long-term outcomes for surgically resected craniopharyngiomas. **Neurosurgery 46:**291–305, 2000
12. Fahlbusch R, Honegger J, Paulus W, Huk W, Buchfelder M: Surgical treatment of craniopharyngiomas: experience with 168 patients. **J Neurosurg 90:**237–250, 1999
13. Habrand JL, Ganry O, Couanet D, Rouxel V, Levy-Piedbois C, Pierre-Kahn A, et al: The role of radiation therapy in the management of craniopharyngioma: a 25-year experience and review of the literature. **Int J Radiat Oncol Biol Phys 44:**255–263, 1999
14. Hardy J, Lalonde JL: Exorese par voie trans-sphenoidale d'un craniopharyngiome geant. **Union Med Can 92:**1124–1129, 1963
15. Harris PE, Perry L, Chard T, Chaudry L, Cooke BA, Touzel R, et al: Immunoreactive human chorionic gonadotrophin from the cyst fluid and CSF of patients with craniopharyngioma. **Clin Endocrinol 29:**503–508, 1988
16. Hoffman HJ: Craniopharyngiomas. The role for resection. **Neurosurg Clin N Am 1:**173–180, 1990
17. Honegger J, Buchfelder M, Fahlbusch R: Surgical treatment of craniopharyngiomas: endocrinological results. **J Neurosurg 90:** 251–257, 1999
18. Honegger J, Buchfelder M, Fahlbusch R, Daubler B, Dorr HG: Transsphenoidal microsurgery for craniopharyngioma. **Surg Neurol 37:**189–196, 1992
19. Hoogenhout J, Otten BJ, Kazem I, Stoelinga GB, Walder AH: Surgery and radiation therapy in the management of craniopharyngiomas. **Int J Radiat Oncol Biol Phys 10:**2293–2297, 1984
20. Kobayashi T, Tanaka T, Kida Y: Stereotactic gamma radiosurgery of craniopharyngiomas. **Pediatr Neurosurg 21 (Suppl 1):**69–74, 1994
21. Konig A, Ludecke DK, Herrmann HD: Transnasal surgery in the treatment of craniopharyngiomas. **Acta Neurochir 83:**1–7, 1986
22. Landolt AM, Zachmann M: Results of transsphenoidal extirpation of craniopharyngiomas and Rathke's cysts. **Neurosurgery 28:** 410–415, 1991
23. Lapras C, Patet JD, Mottolese C, Gharbi S, Lapras C Jr: Craniopharyngiomas in childhood: analysis of 42 cases. **Prog Exp Tumor Res 30:**350–358, 1987
24. Laws ER Jr: Transsphenoidal microsurgery in the management of craniopharyngioma. **J Neurosurg 52:**661–666, 1980
25. Laws ER Jr: Transsphenoidal removal of craniopharyngioma. **Pediatr Neurosurg 21 (Suppl 1):**57–63, 1994
26. Maira G, Anile C, Albanese A, Cabezas D, Pardi F, Vignati A: The role of transsphenoidal surgery in the treatment of craniopharyngiomas. **J Neurosurg 100:**445–451, 2004

27. Maira G, Anile C, Rossi GF, Colosimo C: Surgical treatment of craniopharyngiomas: and evaluation of the transsphenoidal and pterional approaches. **Neurosurgery 36:**715–724, 1995
28. Manaka S, Teramoto A, Takakura K: The efficacy of radiotherapy for craniopharyngioma. **J Neurosurg 62:**648–656, 1985
29. Miller DC: Pathology of craniopharyngiomas: clinical import of pathological findings. **Pediatr Neurosurg 21 (Suppl 1):**11–17, 1994
30. Mokry M: Craniopharyngiomas: a six year experience with Gamma Knife radiosurgery. **Stereotact Funct Neurosurg 72 (Suppl 1):**140–149, 1999
31. Raimondi AJ, Rougerie J: A critical review of personal experiences with craniopharyngioma: clinical history, surgical technique, and operative results. 1983. **Pediatr Neurosurg 21:**134–154, 1994
32. Shirane R, Ching-Chan S, Kusaka Y, Jokura H, Yoshimoto T: Surgical outcomes in 31 patients with craniopharyngiomas extending outside the suprasellar cistern: an evaluation of the frontobasal interhemispheric approach. **J Neurosurg 96:**704–712, 2002
33. Skorzewska A, Lal S, Waserman J, Guyda H: Abnormal food-seeking behavior after surgery for craniopharyngioma. **Neuropsychobiology 21:**17–20, 1989
34. Sorva R, Heiskanen O: Craniopharyngioma in Finland. A study of 123 cases. **Acta Neurochir 81:**85–89, 1986
35. Sung DI, Chang CH, Harisiadis L, Carmel PW: Treatment results of craniopharyngioma. **Cancer 47:**847–852, 1981
36. Sweet WH: Radical surgical treatment of craniopharyngioma. **Clin Neurosurg 23:**52–79, 1976
37. Symon L, Sprich W: Radical excision of craniopharyngioma. Results in 20 patients. **J Neurosurg 62:**174–181, 1985
38. Tarbell NJ, Barnes P, Scott RM, Goumnerova L, Pomeroy SL, Black PM, et al: Advances in radiation therapy for craniopharyngiomas. **Pediatr Neurosurg 21 (Suppl 1):**101–107, 1994
39. Tomita T, McLone DG: Radical resections of childhood craniopharyngiomas. **Pediatr Neurosurg 19:**6–14, 1993
40. Van Effenterre R, Boch AL: Craniopharyngioma in adults and children: a study of 122 surgical cases. **J Neurosurg 97:**3–11, 2002
41. Wara WM, Sneed PK, Larson DA: The role of radiation therapy in the treatment of craniopharyngioma. **Pediatr Neurosurg 21 (Suppl 1):**98–100, 1994
42. Weiner HL, Wisoff JH, Rosenberg ME, Kupersmith MJ, Cohen H, Zagzag D, et al: Craniopharyngiomas: a clinicopathological analysis of factors predictive of recurrence and functional outcome. **Neurosurgery 35:**1001–1011, 1994
43. Weiss MH: The transnasal transsphenoidal approach, in Apuzzo MLJ (ed): **Surgery of the Third Ventricle.** Baltimore: Williams & Wilkins, 1987, pp 476–494
44. Wen BC, Hussey DH, Staples J, Hitchon PW, Jani SK, Vigliotti AP, et al: A comparison of the roles of surgery and radiation therapy in the management of craniopharyngiomas. **Int J Radiat Oncol Biol Phys 16:**17–24, 1989
45. Yaşargil MG, Curcic M, Kis M, Siegenthaler G, Teddy PJ, Roth P: Total removal of craniopharyngiomas. Approaches and long-term results in 144 patients. **J Neurosurg 73:**3–11, 1990

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