Recent results of primary transnasal surgery for infradiaphragmatic craniopharyngioma

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Results of primary transnasal surgery were evaluated in 35 patients (18 males and 17 females) with intrasellar and suprasellar craniopharyngiomas treated between 1985 and 1996 when more refined surgical and diagnostic techniques were available. Patients ranged in age from 8 to 72 years (mean 27 years); 14 patients were younger than 18 years of age. The transnasal approach was chosen because of sellar enlargement and presence of infradiaphragmatic tumor. The paramedian portion of the normal pituitary gland was incised vertically to reach a dorsally located tumor in 25 patients. Complete tumor resection was achieved in 15 patients and subtotal removal in 19; in one patient, only aspiration of cyst contents was performed. Tumor regrowth was seen in three patients after subtotal removal; in two, total tumor removal was achieved by a second transnasal surgery, whereas radiotherapy was administered in the other. In a single patient, total tumor removal was achieved by a second transcranial surgery after cyst aspiration. The duration of the clinical follow-up period was at least 1 year. Persistent diabetes insipidus appeared after total tumor resection in five patients. Cerebrospinal fluid leakage occurred in three patients, with two requiring revision. Among 29 patients with preoperatively normal pituitary functions, 20 (69%) were preserved after primary total resection, whereas six (19.4%) of 31 previously disturbed functions were normalized. After subtotal removal including cyst aspiration, 39 (88.6%) of 44 normal functions were preserved, whereas nine (24.3%) of 37 disturbed functions were normalized. The transnasal approach should be the first choice in infradiaphragmatic craniopharyngiomas with sellar enlargement in cases in which the extrasellar portion is mostly cystic and is accessible. The concept of subtotal removal with preservation of pituitary functions, especially when treating craniopharyngioma in children, seems to be justified.

Key Words * craniopharyngioma * infradiaphragmatic tumor * pituitary function * primary transnasal surgery

The surgical approach of choice for craniopharyngioma, still a matter of debate, is determined by the location and extent of the tumor. Craniotomy via various routes is most commonly used for removal of tumors located in the suprasellar region.[21,23,24] A transsphenoidal approach is chosen when a craniopharyngioma is located either totally or partially within an enlarged sella turcica and has only a limited suprasellar component; several small series concerning this topic have been published.[1,4,7-9,11,13,14,16,20] The anatomical situation makes it more difficult to avoid further damage to the pituitary gland with total tumor removal because the gland has to be incised or dislocated

to access the tumor. Since 1971 we have subtotally resected most of the latter-described tumors via a transnasal approach; the senior author has published the results over the period of 1971 to 1984.[14] Magnetic resonance (MR) imaging, which provides detailed information about tumor location and extent,[22] is extremely helpful in planning the surgical approach. Moreover, pressure-irrigation-suction systems and mirror techniques allow removal of extrasellar tumor components under visual control.[19] To evaluate the effectiveness of improved transnasal microsurgery in our recent cases, we analyzed the results of primary transnasal surgery for intrasellar and suprasellar infradiaphragmatic craniopharyngiomas.

CLINICAL MATERIAL AND METHODS

Patient Population

One hundred twenty-six patients with a histologically confirmed craniopharyngioma underwent surgery at Hamburg University or at the Marienkrankenhaus in Hamburg from January 1985 to December 1996. We review a series of 35 consecutive patients (27.8%) among this group who underwent primary transnasal surgery, including 18 males and 17 females ranging in age from 8 to 72 years (mean $\pm$ standard error, 26.9 ± 2.7). Fourteen patients were younger than 18 years of age. None had undergone any previous surgery or radiotherapy.

Clinical Symptoms

The preoperative duration of symptoms due to tumor varied between 3 weeks and 11 years (mean 2.1 ± 0.4). Principal signs and symptoms included chiasmatic syndromes such as temporal visual field defects in 18 patients and headache in 16. Hypogonadism was the predominant symptom in patients aged 18 years and older, affecting 12 of these 21 patients. Growth delay was the most common symptom in patients younger than 18 years of age, occurring in nine of 14. Four of these nine patients also experienced pubertal delay. Eight patients manifested diabetes insipidus to varying degrees, based on total fluid intake, urine volume, morning urine specific gravity, and clinical criteria, including history. Water-deprivation testing was performed in some borderline cases. Eight patients presented with secondary amenorrhea and two with galactorrhea.

Endocrinological Findings

Endocrinological findings were assessed on the basis of baseline hormonal levels (normal range: prolactin, 1.5-20 ug/L; adrenocorticotrophic hormone [ACTH], 30-60 pg/mL; thyroid-stimulating hormone [TSH], 0.3-3.4 μ U/mL; luteinizing hormone, 6-34 mIU/mL; and follicle-stimulating hormone, 2-22 mIU/mL) and endocrine stimulation tests as needed. For assessment of the hypothalamic-pituitary-adrenal axis (adrenocorticotrophic function), dynamic testing was performed with either corticotropin-releasing hormone stimulation or insulin-induced hypoglycemia and the serum cortisol response measured. For evaluation of the thyroid and gonadal function, dynamic testing with thyrotropin-releasing hormone and gonadotropin-releasing hormone stimulation was performed. Growth hormone (GH) secretion was judged on the basis of endocrinological testing (insulin tolerance test, GH-releasing hormone test, or arginine test), because growth can be normal or even excessive in patients with craniopharyngioma, even if their pituitary gland produces no GH.[2] Nine children showed GH deficiency. Hyperprolactinemia was observed in 13 patients. Further assessment of anterior pituitary function showed adrenal insufficiency in 18, thyroid insufficiency in 10, and gonadal insufficiency in 18 patients (Table 1).

Anterior Pituitary Function	No. of Patients			
	Preop	Postop		
		Normal	Abnormal	No Data
complete tumor removal (15 patients)				
growth hormone				
normal	7	7	0	0
subnormal	7	0	7	0
no data	1	1	0	0
prolactin				
normal	7	7	0	0
elevated	4	3	1	0
no data	4	1	0	3
adrenocorticotrophic hormone				
normal	5	1	4	0
subnormal	8	0	5	3
no data	2	2	0	0
thyrotrophic hormone				
normal	7	4	2	1
subnormal	4	0	4	0
no data	4	1	0	3
gonadotrophic hormone				
normal	3	1	2	0
subnormal	8	3	3	2
no data	4	1	0	3
subtotal tumor removal (20 patients)				
growth hormone				
normal	13	13	0	0
subnormal	2	0	2	0
no data	5	3	0	2
prolactin				
normal	8	8	0	0
elevated	9	4	5	0
no data	3	3	0	0
adrenocorticotrophic hormone				
normal	8	6	2	0
subnormal	10	2	6	2
no data	2	0	0	2
thyrotrophic hormone				
normal	10	7	2	1
subnormal	6	1	4	1
no data	4	1	1	2
gonadotrophic hormone				
normal	5	5	0	0
subnormal	10	2	8	0
no data	5	0	0	5

Radiological Findings

Polytomography scanning showed an enlarged sella turcica in all but one patient and incomplete sphenoid pneumatization in six children. Six patients were studied preoperatively by computerized tomography (CT) scanning, and 29 patients by MR imaging. Radiological examination demonstrated primarily intrasellar masses with moderate suprasellar extension, and an intact diaphragm stretched upward by the tumor in all but one patient. The masses measured between 10 mm and 40 mm in diameter (mean 21.9 ± 1.2). The principal mass was exclusively intrasellar in two (Fig. 1), intrasellar and

suprasellar in 32 (Figs. 2-4), and suprasellar only in one patient. Calcifications (Fig. 4) were found in 13 craniopharyngiomas, and cysts were observed in all. Magnetic resonance T₁-weighted imaging demonstrated a high-intensity cystic tumor in 20 patients and a low-intensity cystic tumor in nine.

Fig. 1. Images obtained in a 13-year-old girl with diabetes insipidus. Left: Preoperative sagittal T₁-weighted MR image revealing a high-intensity intrasellar cystic mass. Right: Postoperative image, 2 years after transnasal surgery, showing complete excision of a craniopharyngioma, with preservation of the pituitary gland and stalk.

Transnasal Surgery

In general, when a craniopharyngioma produces enlargement of the sella, its origin is likely to be intrasellar, below the diaphragm.[10,11] The transnasal approach was chosen when the infradiaphragmatic tumor was located entirely or partly in an enlarged sella and no significant parasellar extension was present. The operative technique representing the transnasal approach to the sellar region has been described in detail elsewhere.[18] In six patients with incomplete pneumatization of the sphenoid bone, adequate exposure was achieved by drilling of the sphenoid (Table 2). In most patients, after achieving wide opening of the dura, the anterior pituitary gland was seen anteriorly within the sella, and the paramedian portion of the normal gland was vertically incised and mobilized laterally to reach the dorsally located tumor. The capsule of the craniopharyngioma behind the pituitary gland then was exposed and opened. After intracapsular debulking, the tumor capsule was dissected from surrounding structures such as the pituitary gland, cavernous sinus, and diaphragma sellae, and the residual capsule was coagulated. The pituitary stalk was not sacrificed in any patient, although sharp dissection of the capsule from the stalk was necessary in some. In addition to intraoperative evaluation by the surgeon, the extent of tumor resection was estimated by postoperative MR imaging.

TABLE 2 FINDINGS IN PATIENTS TREATED WITH TRANSNASAL SURGERY	
Finding	No. of Patients
sphenoid sinus	
conchal type	4
presellar type	2
pituitary gland	
anterior to tumor	25
superior to tumor	10
cyst content	
"machine oil"	17
cholesterin	18

Follow-Up Review

Postoperative endocrinological and ophthalmological evaluations were performed beginning 1 week after surgery. Repeated MR imaging was performed 6 months or less after surgery. For further follow-up review, all patients were seen by referring endocrinologists and pediatricians. The patients were followed clinically and radiologically for 12 to 136 months (mean 24.1 ± 4.7 months).

Fig. 2. Images obtained in a 46-year-old man with hypogonadism, visual disturbance, and headache. Left: Preoperative sagittal T₁-weighted MR image revealing a high-intensity intrasellar and suprasellar cystic tumor, which anteriorly displaces the normal pituitary gland. Right: Postoperative image, 3 years after transnasal surgery, showing total tumor removal, with preservation of the pituitary gland and stalk.

RESULTS

Surgical Findings

Surgical findings are shown in Table 2. The thinned bone of the sellar floor and basal sellar dura were intact in all patients. In 25 patients (71.4%), normal pituitary tissue was recognized anterior to the tumor within the sella after opening the dura, and in all of these patients the gland had to be incised and dislocated in order to reach the craniopharyngioma. In 10 patients, the cysts were located immediately

adjacent to the basal dura, and cyst fluid spilled out when the dura was incised. In such patients, the normal gland was found superiorly to the tumor. The cyst contents had the characteristic "machine oil" appearance in 17 patients and a somewhat purulent appearance approximating cholesterol in 18 others. In two patients, the craniopharyngioma was exclusively intrasellar. Radical removal of the tumor at first operation, with preservation of the normal gland and stalk, was possible in these patients (Fig. 1). In 32 patients, the tumor was intrasellar and suprasellar. Complete removal of the intracapsular tumor and the entire capsule was obtained in 13 patients (Fig. 2); in 19, removal was subtotal (near total). In the latter patients, a portion of the tumor capsule remained in a retrosellar pouch of the diaphragm, and the residual capsule was coagulated (Figs. 3 and 4).

Fig. 3. Images obtained in an 18-year-old woman with secondary amenorrhea and visual disturbance. Upper Left: Preoperative enhanced coronal T₁-weighted MR image revealing a low-intensity intrasellar and suprasellar cystic tumor with a small area of high intensity that was subtotally removed via the transnasal route. Upper Right: Postoperative image, 6 months after surgery, showing residual tumor. Lower: Images demonstrating regrowth of the residual tumor 1 year after surgery (left) and showing no evidence of tumor recurrence 2 years after second total resection (right).

In five of 13 patients with suprasellar calcifications, the calcifications were completely removed. In one patient, the tumor was located immediately above the sella and diaphragm. Because of poor clinical condition and severe visual deterioration, cyst aspiration was performed by a transnasal approach. Six months later the residual suprasellar tumor mass was completely removed by the transcranial route. In all patients, the diagnosis of craniopharyngioma was confirmed histologically by the same pathologist.

Fig. 4. Images obtained in a 16-year-old girl with visual disturbance and headache. Upper: Preoperative coronal T₁-weighted MR image revealing a large, high-intensity intrasellar and suprasellar cystic mass with a large low-intensity area representing calcification. This craniopharyngioma and large calcification were completely resected. Postoperative MR imaging 2 years after surgery showed no evidence of tumor regrowth (not illustrated). Lower: Specimen photograph displaying the large calcification, which was totally removed.

Surgical Complications

Postoperative cerebrospinal fluid (CSF) leakage occurred in three patients. Two patients had undergone complete removal of an intrasellar and suprasellar tumor and required revision via the transnasal route because of the CSF leakage. In one patient with subtotal tumor removal, CSF leakage resolved after continuous lumbar drainage maintained for 72 hours. Postoperative nasal bleeding occurred in two patients and was controlled with nasal tampons. No operative deaths occurred in this series.

Postoperative Endocrinological Findings

Postoperative endocrinological findings according to total and subtotal removal (including cyst aspiration) via primary transnasal surgery for craniopharyngiomas are shown in Table 1. Regardless of the degree of surgical resection, GH secretion remained normal in all 20 previously normal patients; GH secretion was postoperatively deficient in all nine children with GH deficiency prior to surgery. Prolactin secretion remained normal in all 15 previously normal patients. A postoperative normalization of excessive prolactin secretion was seen in three (75%) of four patients with complete tumor removal, and in four (44.4%) of nine with subtotal removal, whereas hyperprolactinemia persisted in six (46.2%) of 13 previously hyperprolactinemic patients. In four (80%) of five patients with total and in two (25%) of

eight with subtotal removal, normal adrenocorticotrophic function developed a disturbance postoperatively; normalization was observed in two with subtotal removal. Normal thyrotrophic function became disturbed after surgery in two (28.6%) of seven patients with complete removal and in two (20%) of 10 with subtotal removal, whereas in one, normalization occurred with subtotal removal. Normal gonadotrophic function became abnormal postoperatively in two patients in whom a complete removal was achieved, and in three (37.5%) of eight with total and two (20%) of 10 with subtotal removal, disturbed gonadotrophic function preoperatively showed normalization postoperatively.

In 15 patients in whom complete tumor resection was achieved, 20 (69%) of 29 preoperatively normal pituitary functions were preserved after the transnasal surgery, whereas six (19.4%) of 31 previously disturbed functions were normalized. In 20 patients in whom subtotal removal was accomplished, 39 (88.6%) of 44 normal pituitary functions were preserved after surgery, whereas nine (24.3%) of 37 disturbed functions were normalized.

Recurrence, Regrowth, and Adjuvant Therapy

No recurrence has been observed in any patient whose tumor was totally removed. Regrowth of the tumor was seen in three patients (8.6%) in whom the tumor had been subtotally removed. In two patients, the regrown tumor was completely resected by a second transnasal procedure 12 to 41 months after the first operation (Fig. 3). In one patient, radiotherapy was performed 6 months after surgery; this patient has no evidence of tumor progression 6 years later.

Patient Outcomes

Fifteen of 18 patients with visual disturbances regained normal visual function, and the remaining 3 showed significant improvement within three months after surgery. Headache completely resolved after surgery in all patients. Eleven patients were found to have newly diagnosed diabetes insipidus after primary surgery. The diabetes insipidus was persistent in five patients; in these five patients, complete tumor resection had been achieved. In eight patients with preexisting diabetes insipidus, the replacement dose of vasopressin could be lowered postoperatively, although diabetes insipidus had not completely resolved. Secondary amenorrhea was improved in six of eight patients. Galactorrhea resolved in two of two patients. Growth delay was still present in nine children after surgery and GH replacement therapy was required. Pubertal delay remained unchanged postoperatively.

DISCUSSION

Approximately one-third of all craniopharyngiomas reported in the literature involve the pituitary fossa.[1,14,15,20] In our recent series, 27.8% of all patients with craniopharyngiomas had sellar involvement. The transsphenoidal approach is the optimum procedure for intrasellar and suprasellar infradiaphragmatic craniopharyngiomas. In general, it has been suggested that an enlarged pituitary fossa is a prerequisite for transsphenoidal removal of craniopharyngiomas.[4,9,11,14,16,20] However, Honegger, et al.,[13] have maintained that this notion should be modified, and they frequently found slight or no enlargement of the pituitary fossa in their series. In our series, we noticed that the pituitary fossa was slightly enlarged in most cases. We agree with other authors that this approach should be used for infradiaphragmatic craniopharyngiomas and those encasing optic chiasma, hypothalamus, or vascular structures should not be resected by this procedure.[13,23] However, the same authors also stress that if suprasellar calcifications of craniopharyngiomas are detected, complete tumor resection is unlikely, and a transcranial approach will be necessary to accomplish complete excision. Five of 13 craniopharyngiomas

with suprasellar calcifications in our series were completely resected transnasally using pressure-irrigation-suction systems and mirror techniques (Fig. 4).

Maira, et al.,[20] have reported that incision of the normal pituitary gland to reach a craniopharyngioma never resulted in major functional damage to the anterior pituitary. In our series, six (24%) of 25 patients in whom a vertical incision of the pituitary was made to reach a dorsally located tumor had partial pituitary deficiencies involving at least one function; five of these six patients developed adrenocorticotrophic dysfunction. Honegger, et al.,[13] found in most of their patients that, after primary transsphenoidal surgery, anterior pituitary function generally was unchanged except for normalization of hyperprolactinemia. As shown in Table 1, 59 (80.8%) of 73 preoperatively normal pituitary functions were preserved after primary transnasal surgery, whereas for 15 (22.1%) of 68 with preoperative pituitary dysfunction in at least one axis, functions normalized postoperatively. It is noteworthy that GH and prolactin secretion remained normal in 20 and 15 preoperatively normal patients, respectively. Postoperative normalization of prolactin secretion was seen in seven (53.9%) of 13 patients; it was more frequent in complete tumor removal (75%) than in incomplete removal (44.4%). Disturbance of ACTH, TSH, luteinizing hormone, and follicle-stimulating hormone secretion was seen more frequently after complete tumor removal than after incomplete removal. Postoperative normalization of ACTH and TSH secretion was observed only after subtotal resection. Carmel[3] and Laws[17] have observed that careful removal of the tumor capsule does not necessarily cause any additional damage to hypothalamic structures. In our own results, complete tumor removal by the transsphenoidal route carried considerable risk of diabetes insipidus. We have to mention that direct postoperative lumbar drainage was not routinely performed. Therefore, in treating childhood craniopharyngioma, relatively conservative surgery may be desirable in order to preserve normal pituitary tissue and avoid a cognitive defect.[5,6] If tumor is found to be adherent to the hypothalamus at operation, we sometimes consider a staged conservative procedure.

Some authors have reported no tumor recurrences after primary complete resection.[13,17,20,24] As an additional evaluation of surgical resection, we have used enhanced MR imaging 6 months after surgery.[12] In our patients with MR-confirmed total resection, no evidence of tumor recurrence has been found during the limited follow-up period. In contrast, regrowth was observed in only three (15.8%) of 19 patients with incomplete tumor removal, which also involved a lower risk of pituitary damage.

Our study confirms that primary transnasal surgery for infradiaphragmatic craniopharyngiomas with enlarged sella represents the safest approach and is associated with a low operative morbidity. The main disadvantage of this procedure is the risk of CSF leakage. These infradiaphragmatic craniopharyngiomas cannot be compared with supradiaphragmatic craniopharyngiomas, in which total removal by the transcranial route is associated with considerable morbidity and mortality.[24]

Results of primary transnasal microsurgery in two separate series are shown in Table 3. In the earlier series,[14] reduction of tumor bulk was the aim, accomplished by aspiration of cyst contents or subtotal tumor excision. In patients who underwent aspiration of cyst contents, the suprasellar portion of the tumor was larger than the intrasellar one. After aspiration, ⁹⁰yttrium was implanted into the cyst. Presently, MR imaging provides more detailed information about tumor location and extent[22] and is extremely helpful in choosing the most appropriate surgical approach. Therefore, in this more recent series, total or nearly total tumor removal was intended, whereas mere transnasal cyst aspiration was performed in only one patient in poor general condition who had a suprasellar craniopharyngioma without sellar enlargement.

TABLE 3 RESULTS OF PRIMARY TRANSNASAL MICROSURGERY FOR CRANIOPHARYNGIOMAS IN TWO SEPARATE SERIES			
		König, et al. 1971–1984	Present Series 1985–1996
no. of patients		29	35
sex (male/female)		18:11	18:17
age range (yrs) (mean)		7–48 (25)	8–72 (27)
operation			
cyst aspiration	primary	7	1
	reop	5	1
subtotal removal	primary	20	19
	reop	1	2
	radiation	1	1
complete removal	primary	2	15
	reop	0	0
radiation therapy		1	1
surgical complications	CSF leakage	2	3
	revision	1	2
	oculomotor nerve palsy	1	0
mortality		1	0

Results of primary transsphenoidal surgery for craniopharyngiomas in other reported series are shown in Table 4. Difficulties arise in comparing our recent series with other reports because of variation in location and extent of tumor, surgical strategy, and follow-up intervals. Nevertheless, our results do not differ greatly from other recent series from academic institutions.

TABLE 4 RESULTS OF PRIMARY TRANSPHENOIDAL SURGERY FOR CRANIOPHARYNGIOMAS IN OTHER REPORTED SERIES						
Authors & Year	No. of Patients	Surgical Removal			Surgical Mortality	Reoperation
		Total	Subtotal	Cyst Aspiration		
Hardy & Vezina, 1976	9	3	2	4	0	4/9 (44%)
Garcia-Uria, 1978	4	no data	no data	no data	1/4 (25%)	no data
Laws, 1980	14	9	5	0	1/14 (7%)	0
Grisoli, et al., 1982	9	no data	no data	no data	0	2/9 (22%)
Baskin & Wilson, 1986	29	no data	no data	no data	no data	no data
König, et al., 1986	29	2	20	7	1/29 (3%)	6/29 (21%)
Landolt & Zachmann, 1991	9	no data	no data	no data	1/9 (11%)	3/9 (33%)
Honegger, et al., 1992	19	15	4	0	0	3/19 (16%)
Maira, et al., 1995	35	23	12	0	0	6/35 (17%)
current series, 1997	35	15	19	1	0	3/35 (9%)

CONCLUSIONS

In conclusion, the transnasal approach should be the first choice in intrasellar and suprasellar infradiaphragmatic craniopharyngiomas with sellar enlargement if the extrasellar component is mostly cystic and readily accessible. The concept of subtotal tumor excision for better preservation of the pituitary functions, especially when treating childhood craniopharyngiomas, seems to be justified, whereas mere aspiration of cyst contents had a mostly a transitory effect.

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