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INVITED PAPER

Craniopharyngiomas in children: how radical should the surgeon be?

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Abstract
Purpose Two main modes of management of craniopharyngiomas, namely, radical tumor removal and intentional incomplete removal followed by radiotherapy, are used. Recently, a half-way solution was added. Radical removal is reserved only for the tumors not involving hypothalamus. Such tumors, however, are not clearly defined. The goal of the study was to clarify the relationship of craniopharyngiomas with surrounding structures, especially hypothalamus, and to evaluate its clinical significance.
Methods Our policy of management of craniopharyngiomas was elaborated on the basis of the results of morphological studies of the topography and their correlation with magnetic resonance imaging (MRI) in 115 adults and children operated on since 1991. Suitability of the policy in children and adolescents was verified by long-term outcome analysis in 41 consecutive patients.
Results The rate of morbidity and mortality was higher in patients with craniopharyngiomas located inside the third ventricle either partially (intraventricular and extraventricular craniopharyngiomas, IEVCs, 16 patients) or completely (intraventricular, one patient) than in tumors located outside the ventricle (suprasellar extraventricular, SEVCs, five patients; intrasellar and suprasellar, 19 patients). Postsurgical hypothalamic signs and symptoms occurred most often in intraventricular tumors; there were no mental disorders or obesity caused by primary removal of SEVCs including those severely compressing hypothalamus.
Conclusions Radical removal of SEVCs is safer than of IEVCs despite an apparent involvement of hypothalamus. In majority of cases, they may be distinguished by indirect MRI signs; in others only according to operation findings; final decision about the optimal extent of tumor removal should be made during surgery.

Keywords Pediatric craniopharyngioma · Extent of resection · Hypothalamus · Surgical outcome

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Introduction

Craniopharyngiomas, benign extra-axial epithelial tumors, often follow an aggressive clinical course resulting in significant morbidity and shortened life expectancy. The most logical treatment seems to be total tumor removal and thus cure of the patient.

The intention to remove the craniopharyngioma totally whenever possible emerged in the past in conjunction with therapeutic and diagnostic improvements: steroid hormone replacement, microsurgery, magnetic resonance imaging [3, 8, 13, 18, 21, 30, 32, 41, 47, 48]. However, radical tumor removal led to a relatively high rate of surgical morbidity and also to surgical deaths. Therefore, another approach to the management of craniopharyngiomas especially in children, namely, intentional incomplete removal followed by radiotherapy, has been advocated [15, 35]. Radiotherapy lowered the rate of recurrences but failed in some series [42] and moreover caused adverse effects [8, 28, 30, 34]. The possibilities of radiosurgery and of intracystic brachytherapy are limited in immediate vicinity of the structures of the visual pathway [4, 44]. A combination of intracystic chemotherapy and brachytherapy led to a high rate of complications [14]. Then, a

compromised solution has been elaborated: radical removal was recommended only for the patients harboring the tumors not involving hypothalamus [27, 31]. "Involvement of hypothalamus" was defined by retrochiasmatic growth of the tumor towards the hypothalamus with the latter no longer identifiable on preoperative magnetic resonance imaging (MRI) scan. Such an image, however, does not indicate whether the hypothalamus is compressed or destroyed and what is the nature and intensity of the adherence of the tumor to diencephalic structures [37, 39].

The aim of the study was to evaluate our treatment policy regarding craniopharyngiomas in children and adolescents which was worked out on the basis of both morphological studies [37] and correlation of morphological data with neuroradiological and operative findings [39].

Patients and methods

In 1991, MRI became available to our practice which was crucial in revealing the topography of the tumor and also for objectively assessing the extent of its removal. Since then, 115 consecutive patients with craniopharyngiomas have been operated on, 41 out of them were children and adolescents less than 18 years of age. The age of 21 boys and 20 girls at the time of surgery ranged from 11 months to 17 years, mean 9.3 years. Four of them had recurrent tumors primarily operated elsewhere; three of the latter were irradiated before referral to our department.

According to the relationships of the tumors to the sella and its diaphragm, they were classified as infradiaphragmatic or supradiaphragmatic. All infradiaphragmatic craniopharyngiomas secondarily extended outside the enlarged cavity of the sella and were thus intrasellar and suprasellar (ISCs) in location. Supradiaphragmatic, i.e., primarily suprasellar, tumors were further subdivided according to their relationship with the floor of the third ventricle (3rd VF) into the following topographic groups: suprasellar extraventricular (SEVCs), intraventricular and extraventricular (IEVCs), and purely intraventricular (IVC) craniopharyngiomas. Topographical relationships of the tumor with surrounding structures as revealed by MRI served as the basis for the choice of surgical approach and surgical tactics. According to their size, the tumors were classified as small if their greatest diameter reached 2 cm or less, medium-sized if more than 2 cm up to 4 cm, large if more than 4 cm up to 6 cm, and giant if larger than 6 cm (Table 1).

Tumor removal was considered radical if the intraoperative impression of the surgeon based on the view through the operative microscope and, if necessary, through a straight and/or angled endoscope was confirmed by postoperative MRI performed 3 months after surgery. If a small tumor remnant not exceeding 10% of its original volume was found, the extent of tumor removal was classified as subtotal. In a patient in whom a small part of the tumor capsule was left, the removal was classified as subtotal even if it could not be detected on postoperative MRI scans. In patients with larger tumor remnants, the resection was classified as partial. After radical tumor removal, MRI examinations were thereafter repeated on a yearly basis. The intervals between subsequent MRI examinations in patients with residual tumor were modified according to the findings at the last examination and to the result of their comparison with previous neuroradiological data.

Forty patients who survived surgery were followed for 2–227 months, mean 123 months; six of them died in later periods. Thirty-four patients are now alive with a range of 9–227 months, mean 138 months after surgery. Clinical and radiological outcome at the end of the follow-up was evaluated separately in each topographic group. The recurrence and the survival rates were also analyzed separately for the patients primarily operated in our department. These patients were never irradiated prior to repeated surgery for recurrence. All patients were followed by endocrinology, ophthalmology, and neurosurgery. In cases where cognitive disorders or other mental disturbances were suspected, neuropsychological and/or psychiatric examinations were also performed. For evaluation of the visual acuity, we designed a five-grade scale: normal, functionally normal (greater than or equal to 0.5 but less than 1.0) [2], worsened (greater than 0.1 but less than 0.5 with ability to read), functionally blind (0.1 or less) [40], and blind.

Table 1 Size of the tumors according to the greatest diameter

Type of tumor	Small (up to 2 cm)	Middle-sized (up to 4 cm)	Large (up to 6 cm)	Giant (>6 cm)	Total
Intrasellar and suprasellar	1	12	6		19
Suprasellar extraventricular	1	1	1	2	5
Intraventricular and extraventricular	1	3	10	2	16
Intraventricular		1			1
Total	3	17	17	4	41

Results

In 19 patients, ISCs were found (three of them recurrent), five patients had SEVCs, and the rest had tumor located inside the third ventricular chamber either partially—IEVCs in 16 patients (one of them recurrent)—or completely—IVC in one patient.

Intrasellar and suprasellar craniopharyngiomas

Craniopharyngiomas originating within the sellar cavity enlarged the sella and pushed its diaphragm upwards similar to pituitary adenomas. The suprasellar part of the tumor sometimes reached a large size and displaced the optic chiasm as well as the third VF superiorly (Table 1). Seven tumors were approached transsphenoidally. Compressed anterior pituitary was found and preserved in five of them. In 12 patients, the tumor was exposed via unilateral subfrontal approach. Decision for craniotomy was made because of a large size of suprasellar part of the tumor extending beyond the region of the sella, or its dumbbell shape, or less often because of undeveloped sphenoid sinus in a small child (Fig. 1). After reaching the tumor below the frontal lobe and its partial removal or emptying of the cyst, the chiasm was found on a superior or anterior–superior surface of the tumor; exposure of the latter therefore was sufficient. The arachnoid located between the upper pole of the tumor and the overlying anatomical structures facilitated radical tumor removal. In one patient with a large almost exclusively retrochiasmatic tumor reaching the roof of the third ventricle, enlargement of the lateral ventricles was revealed. Intraventricular extension of the tumor was therefore suspected. However, thinned out and stretched third VF gradually descended down during tumor removal. Its perforation could not be confirmed by means of the endoscope after removal of the most posterior superior part of the tumor.

Radical excision could be achieved in 15 of 16 primarily operated patients (Table 2). The cause of incomplete removal in one patient was a firm adherence of its capsule to the A1 segment of the anterior cerebral artery which led to intraoperative injury of the vessel. A small opening of the vessel was closed by a tangentially placed clip without clinical consequences. Three tumors primarily operated elsewhere were removed incompletely because they adhered to multiple surrounding structures. The pituitary stalk was identified and preserved in four of 12 craniotomies and in all six primary transsphenoidal operations. Only three of ten patients with preserved stalk, however, had no diabetes insipidus. Preservation of the remnants of anterior pituitary was achieved in five of 19 patients. All of them needed at least partial hormonal replacement (Table 3).

There was no early or late operative mortality; all 19 patients were alive at the end of the follow-up (9–224, mean 128 months). Preoperative obesity in one patient persisted; three patients became obese after surgery. At least in one female patient it could not be attributed to hypothalamic lesion. The tumor was small; it reached the chiasm but not the third VF. The remnants of the anterior pituitary were identified and preserved during transsphenoidal radical tumor removal; she had partial anterior pituitary (thyrotrophic, gonadotrophic) insufficiency. The patient gained 10 kg 4 years after surgery when she was 18 years old and her body weight remained the same for the next 3 years till the end of the follow-up. Preoperative mild memory disturbances and difficulty with concentration in a 10-year-old girl resolved after surgery. Attacks of inappropriate aggressive behavior in a girl 2 years of age also disappeared after surgery. There were no cognitive defects or other mental problems at the end of the follow-up in patients with ISCs.

Visual functions improved in three, remained at preoperative level in 14, and worsened in two patients (Table 4). In the latter two patients with a large tumor, severe visual impairment was present before surgery. Visual acuity at the end of the follow-up was lower than in any other topographic group. The only two patients in the entire pediatric series who needed magnifying loupes for reading had ISCs (Table 5).

Three tumors primarily operated elsewhere did not recur after secondary surgery. Two of them were irradiated before referral to our department; the third one was operated on only 9 months before the end of the follow-up. Out of 16 primarily operated patients followed for 57–224 (mean 139) months, the tumors recurred in two, both after radical removal through craniotomy. The recurrent tumor in both patients was removed radically using the original approach, one in 24 months and another one twice in 44 and 120 months after primary surgery. Both patients are tumor-free without oncology treatment. The patient with a small residual of the tumor capsule has no recurrence for 110 months without adjuvant treatment.

Suprasellar extraventricular craniopharyngiomas

All five patients with SEVCs were operated primarily in our department. The tumors were located above the sellar diaphragm within the subarachnoid space. Large and giant tumors (Table 1) completely or almost completely occluded the third ventricle and the hypothalamic structures could not be identified on MRI scans (Figs. 2 and 3). However, the lateral ventricles were not enlarged; the cerebro-spinal fluid continued to flow through the extremely compressed cavity of the third ventricle above its floor distended on the upper surface of the extraventricular tumor.

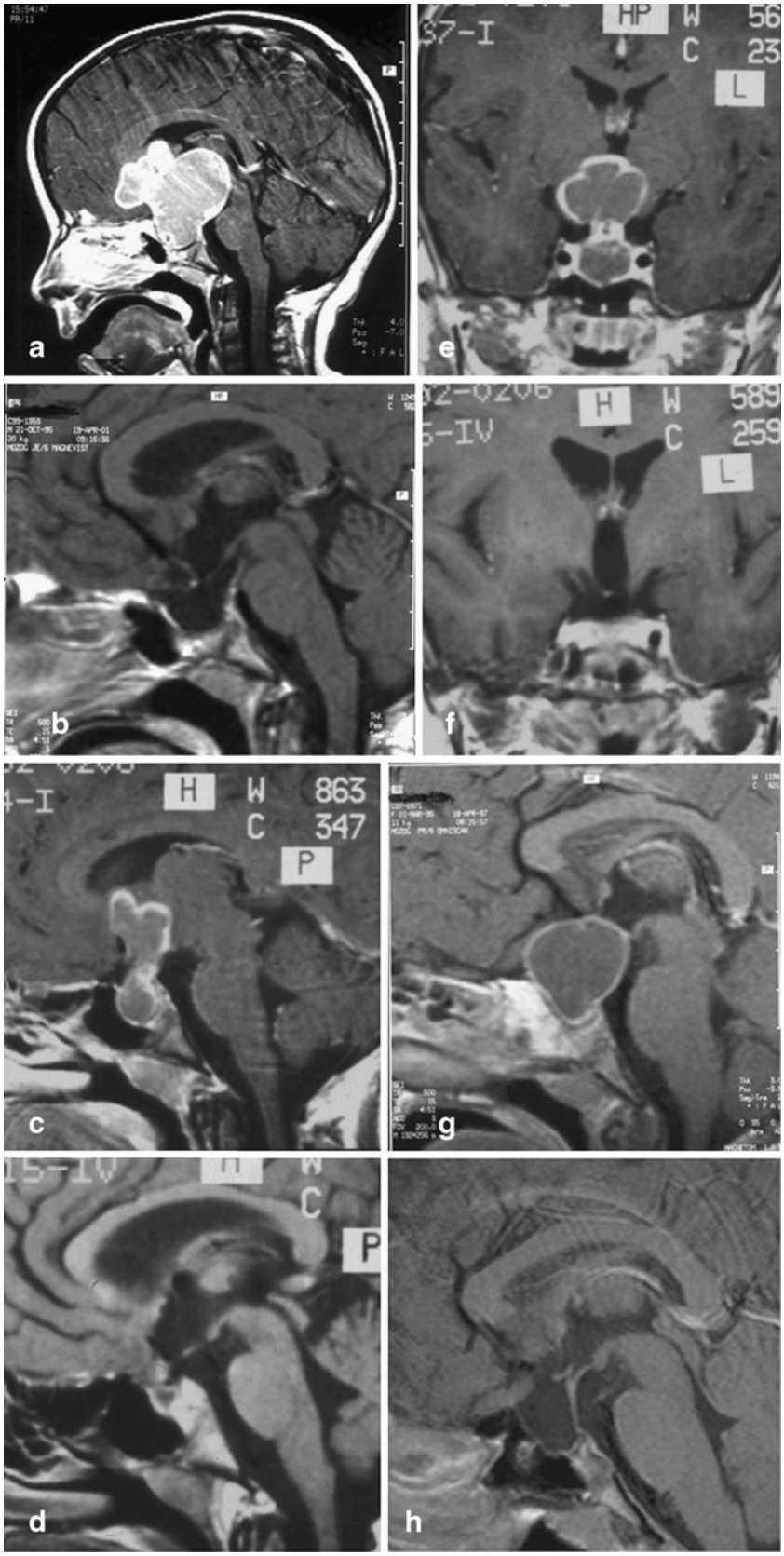

Fig. 1 Intrasellar and suprasellar craniopharyngiomas resected through craniotomy because of a large tumor size (**a**, **b**), dumbbell-shaped (**c**–**f**), and undeveloped sphenoid sinus (**g**, **h**)

Table 2 Surgical approaches and the extent of craniopharyngioma removal

Type of tumor	Approach	Extent of removal			Total
		Radical	Subtotal	Partial	
Intrasellar and suprasellar	Transsphenoidal	6	1 (r)		7
	Subfrontal	9	2 (1r)	1 (r)	12
Suprasellar extraventricular	Subfrontal	2	1		3
	Bifrontal	1			1
	Pterional	1			1
Intraventricular and extraventricular	Trans LT	6			6
	Trans CC	2 (1r)			2
	Combined	4	3	1	8
Intraventricular	Trans LT		1		1
Total		31	8	2	41

r recurrent tumor, *Trans LT* trans-lamina terminalis, *Trans CC* transcallosal

In three patients, the tumor was resected through unilateral subfrontal approach. Exposure of the tumor below the optic chiasm was sufficient; a giant tumor could be removed only subtotally as its capsule firmly adhered to the pia mater of the infundibulum and the tuber (Table 2). A giant tumor in another patient extending to both sides (Fig. 3) necessitated large bifrontal approach. In the last patient, the entire tumor was located behind the optic chiasm and the pituitary stalk; therefore, more lateral exposure via pterional craniotomy was necessary. The pituitary gland compressed below the sellar diaphragm was left alone in all patients. The pituitary stalk could be identified three times; in two patients, it was preserved. Complete anterior pituitary functions were preserved in just one patient; diabetes insipidus was avoided in one of them as well (Table 3).

There was no surgical mortality. One patient, a girl operated on at the age of 11 months, died later from repeated recurrences. The tumor recurred in 32 months after primary radical surgery and was again removed radically. The next recurrence occurred in another 16 months. Because of severe adherence to all surrounding structures, only partial removal was possible. Subsequent LINAC radiosurgery kept the tumor stable for the rest of her life. In 65 months after the first surgery, the tumor recurred in temporal region. Its radical removal was followed by external radiotherapy. However, the disease continued to progress later on. In 90 months, the tumor recurred in posterior fossa and was radically removed. She was practically blind from the preoperative period and became obese after repeated surgeries. The patient died after 101 months of the follow-up. A single subtotally removed tumor in another patient progressed in 46 months and was again subtotally removed. The remnant is now stable for 13 years without irradiation.

At the end of the follow-up (range 73–202 months, mean 130 months), visual functions improved in two of four survivors and remained stable on preoperative level in two others (Table 4). In one of the patients, an 11-month-old boy, preoperative ophthalmological examinations revealed "practical blindness" with paradoxical reaction to light. Five years after surgery, vision was recovered substantially with the visual acuity of the left eye reaching 5/7.5 and light perception on the right (Table 5). There was no postsurgical weight gain in any of the four survivors. Behavior and memory disorders which led to worsened performance at school before surgery in one child improved after subtotal tumor removal.

Table 3 Functional outcome after craniopharyngiomas resection at the end of the follow-up

Type of tumor	Hypopituitarism			Diabetes insipidus	Obesity	Cognitive/mental disorders	Survivors
	None	Partial	Complete				
Intrasellar and suprasellar	2	3	14 (3r)	16 (3r)	4		19
Suprasellar extraventricular	1		3	3			4
Intraventricular and extraventricular			10	10	6	1	10
Intraventricular		1		1	1		1
Total	3	4	27	30	11	1	34

r recurrent tumor

Table 4 Visual outcome after craniopharyngiomas resection at the end of the follow-up

Type of tumor	Visual functions			Number of survivors
	Improved	Unchanged	Worsened	
Inrasellar and suprasellar	3	14	2	19
Suprasellar extraventricular	2	2		4
Intraventricular/ extraventricular	2	7	1	10
Intraventricular		1		1
Total	7	24	3	34

Intraventricular and extraventricular craniopharyngiomas

In 16 patients, the upper portion of the tumor (one recurrent, 15 primary) was located inside the cavity of the third ventricle and its lower part in the suprasellar space. The border between the intraventricular and the extraventricular portions of the IEVC was represented by a circle created by neural structures located along the tumor's "equator": the chiasm on the anterior (or lower anterior) pole of the tumor, the remnants of the tuber on the tumor's lateral surfaces, and compressed and atrophied mamillary bodies on a posterior (or lower posterior) pole of the tumor (Fig. 4). In minority of cases, the infundibulum was spared; it was stretched over the lower anterior surface of the tumor just behind the chiasm. The central part of the tuber was completely atrophied in all but one case; the lower pole of the tumor was covered only by pia mater continuing from the lateral parts of the tuber. In one patient, practically complete third VF was found without clear connection between the intraventricular and the extraventricular parts of the tumor.

The extraventricular portion of the tumor, by principle, could be removed via basal extracerebral approaches. However, its exposure between the optic nerves was rarely possible because of the low position of the chiasm located immediately on the sellar tubercle hiding the lower anterior surface of the tumor. The approach along the lateral border of the chiasm, medially from the supraclinoid internal carotid artery, and anteriorly from the initial part of the anterior cerebral artery in majority of cases was extremely limited and, in some patients, this so-called optic–carotid triangle was not opened at all. A small part of the tumor could usually be exposed laterally to the carotid artery. Thus, in practice, the extraventricular part of the tumor had to be exposed though the anterior wall of the third ventricle, the lamina terminalis. Opening the lamina terminalis between the chiasm and the anterior communicating artery (AComA) provided good exposure of the entire extraventricular part of the IEVC and the anterior and the basal portion of its intraventricular part. This approach was used in 14 patients (Table 2), and in six of them it was sufficient for appropriate exposure of the whole tumor. However, the most posterior part of the tumor lying in the posterior or posterior superior part of the third ventricle in some patients was hidden from direct view, especially if the position of the AComA was low. This part of the tumor could be reached by opening the lamina terminalis above the AComA; however, in these cases, we preferred its exposure through a short anterior callosotomy (up to 20 mm) just behind the genu. In eight patients, combined transcallosal and trans-lamina terminalis approach through one large frontal craniotomy was used (Fig. 5). In two other patients, anterior callosotomy was sufficient for the entire tumor resection.

In places where the tumor came in contact with the brain tissue either at the posterior angle of the optic chiasm or at the floor and the lateral walls of the third ventricle, no leptomeningeal structures could be found between them and the tumor. Tumor parenchyma, its gliotic capsule, and the remnants of the third VF in some regions apparently

Table 5 Visual acuity after craniopharyngiomas resection at the end of the follow-up

Visual acuity of each eye	Intrasellar/ suprasellar	Suprasellar/ extraventricular	Intraventricular/ extraventricular	Intraventricular	Total
N–N	11	3	5	1	20
N–FN	1		3		4
N–FB		1			1
FN–FN	3		1		4
FN–W	1				1
FN–FB	1		1		1
W–FB	1				1
FB–B	2				2

N normal, *FN* functionally normal (below 1.0 and better or equal to 0.5), *W* worsened, able to read (below 0.5, better than 0.1), *FB* functionally blind (0.1 or less), *B* blind

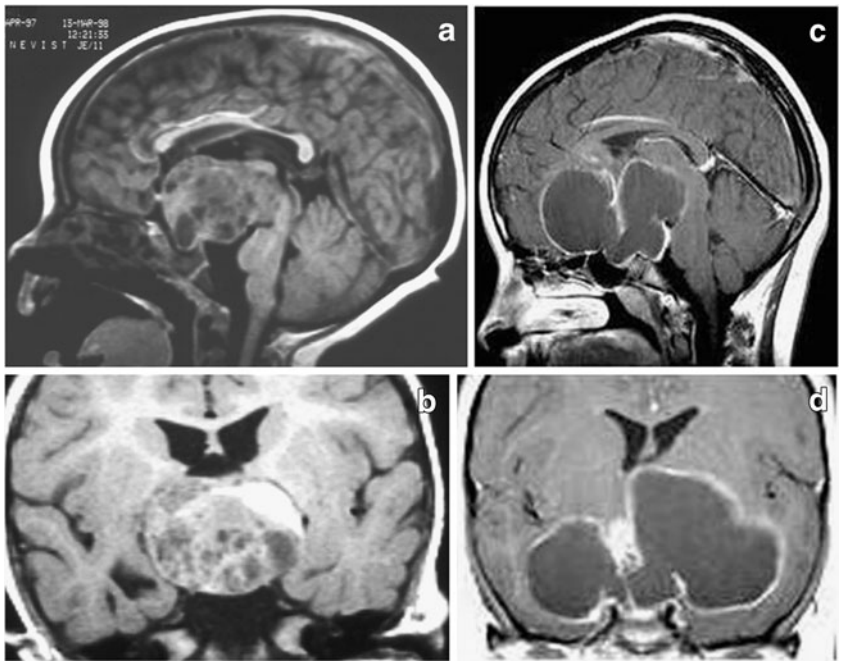

Fig. 2 Suprasellar extraventricular craniopharyngiomas located fully (**a**, **b**) and partially (**c**, **d**) retrochiasmatically. Note the absence of hydrocephalus

formed one layer of tissue. More superiorly, the tumor usually only touched the lateral walls of the third ventricle and could be easily detached from them. Pulling this part of the tumor disclosed the border between the tumor and the diencephalic structures in majority of the patients. If a clear plane of cleavage could be found more basally (at the "hypothalamic ring"), blunt and sharp dissection allowed the removal of the tumor tissue. In some cases, however, no clear border with a plane of cleavage was found and the remnant of the tumor had to be left in place. The tumor was removed radically in 12, subtotally in three and partially in one patient (Table 2).

Despite the careful and apparently safe dissection of the tumor from the hypothalamic structures, severe acute hypothalamic insufficiency occurred in three patients (one after subtotal two after radical removal) during the postoperative period. Neurointensive care was directed by pediatric intensivists, and maintenance of the electrolyte and fluid balance and hormonal replacement were successful in two patients; one child, however, died on the seventh postoperative day. An immediate postoperative course in another patient after subtotal tumor removal was complicated by hemorrhage into the third ventricle which led to severe postoperative course and later on to chronic hypothalamic insufficiency.

During the follow-up of 2–227 (mean 107) months, five patients died: four after primary surgery and one after reoperation. The latter was admitted to our department with severe memory disturbances and endocrine insufficiency 9 years after initial surgery and subsequent numerous interventions performed elsewhere (repeated tumor resections, stereotactic cyst aspirations, shunt implantation and revisions, repeated brachytherapy with radioactive yttrium, and external radiotherapy). Radical removal of a giant tumor via originally performed callosotomy, however, did not improve her condition substantially. She died 7 months after surgery from a concurrent disease.

Fourteen patients with primary IEVCs who survived primary surgery were followed for 2–227 (mean 121.6) months. Three of them died (two after incomplete and one after radical tumor removal) during the initial period of the study (in the years 1992–1995) from complications based mostly on inappropriately managed chronic hypothalamic insufficiency within 1 year after surgery. The fourth patient died 8 years after radical tumor removal. He received hormonal replacement for panhypopituitarism; his vision improved. He attended a special education school because of attention–concentration difficulties and episodes of emotional unstableness although his memory and learning abilities were above average. Because of aggressiveness, he was admitted to a psychiatric department where he died in sleep from "intracranial hemorrhage"; neither neuroradiological imaging nor autopsy was performed.

During the follow-up, seven tumors recurred in 5–118 months after first surgery: six after radical and one after subtotal tumor removal. All were reoperated—six out of seven using previous surgical approaches. One that was originally IEVC recurred within the sellar cavity and was removed by transsphenoidal route. None of the surgeries for recurrent tumor deteriorated the patient's condition.

At the end of the follow-up, ten out of 15 primarily operated patients were alive: eight out of 11 with radical surgery and two out of four with subtotal or partial tumor removal. All survivors are tumor-free after radical tumor

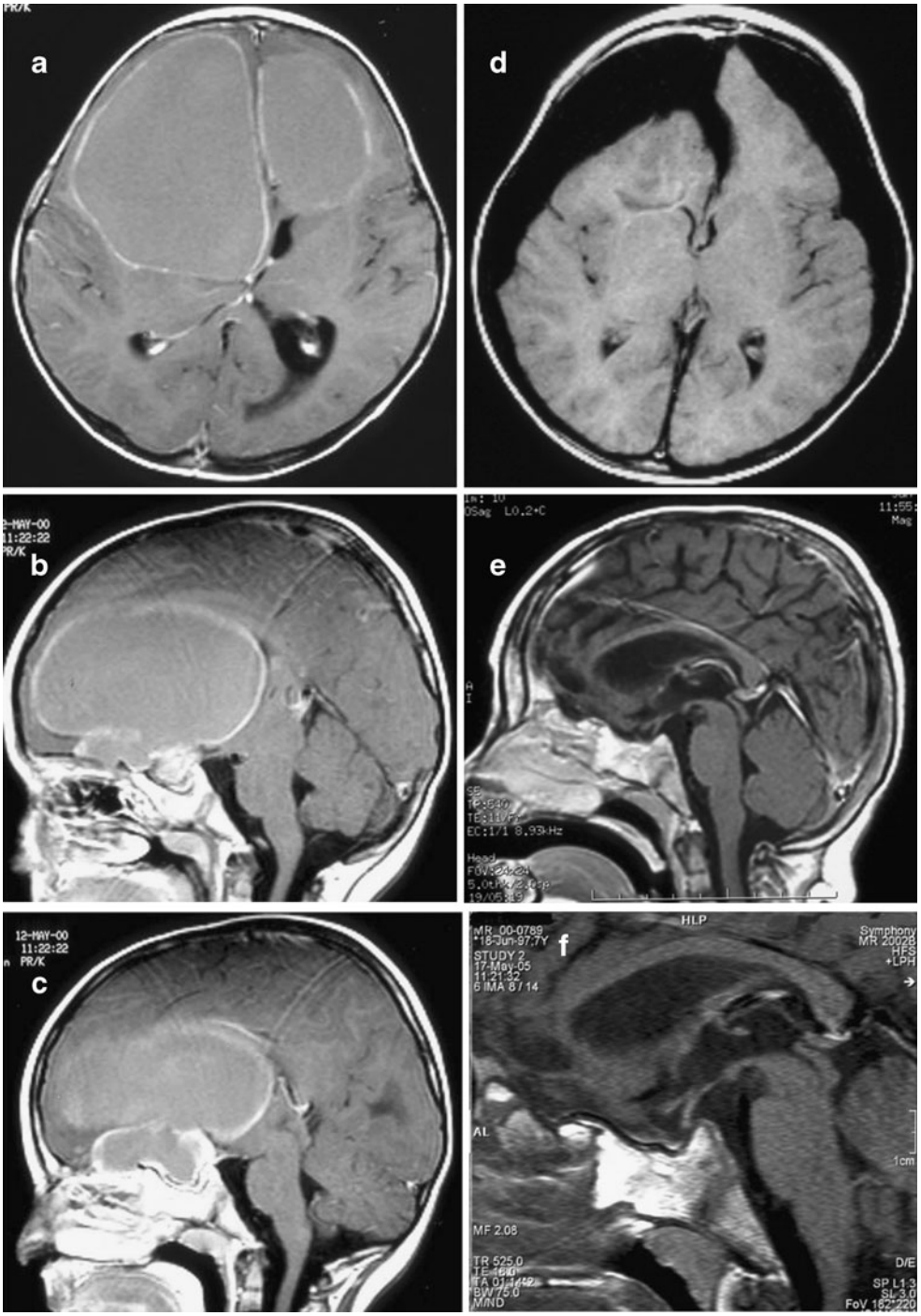

Fig. 3 Giant suprasellar extraventricular craniopharyngioma (**a**–**c**) at 2 days (**d**), 3 years (**e**), and 5 years (**f**) after radical removal via bifrontal craniotomy

removal—six of them after repeated surgery for recurrence. In one of them, the local pediatric oncologist indicated external radiotherapy immediately after radical reoperation. The others received no oncology treatment. After subtotal removal, one patient has a small calcified tumor remnant at the mamillary body which has been stable for 18 years without any further treatment. The other patient received radiosurgery after the third surgery for tumor recurrence; however, it progressed later on and was removed radically in another 23 months (64 months after primary surgery).

All survivors needed hormonal replacement for panhypopituitarism and diabetes insipidus (Table 3). Visual functions improved in two, remained stable on the preoperative level in seven, and worsened in one patient (Table 4). All of them had at least functionally normal visually acuity in one eye (Table 5). Six patients after radical surgery became obese; they gained weight mostly after reoperations, one after chemotherapy for a spinal neoplasm administered 5 years after radical tumor removal. She also developed mild memory disturbances and had to

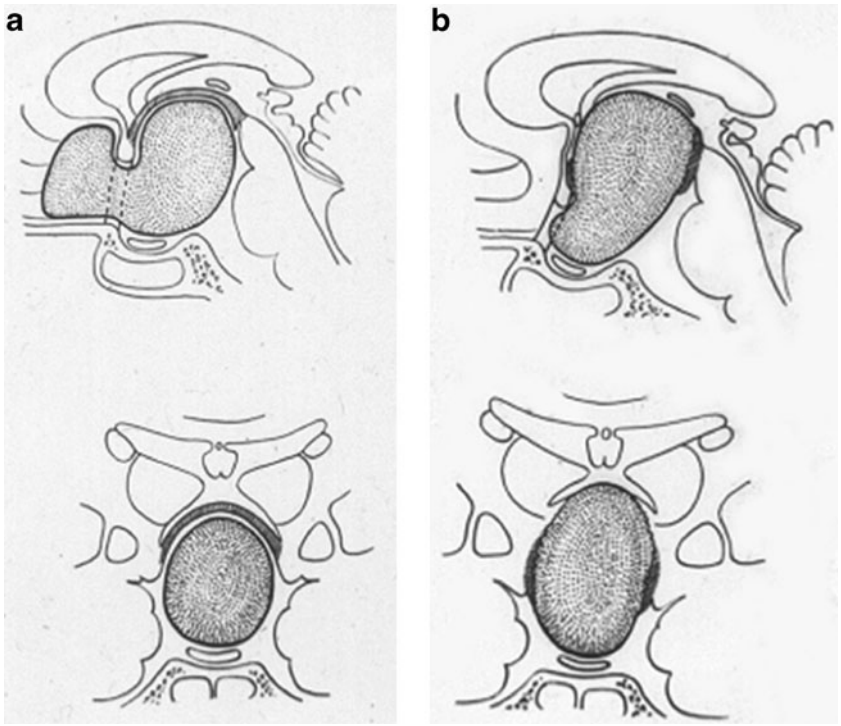

Fig. 4 Schematic representation of the relationships of the suprasellar extraventricular (**a**) and the intraventricular and extraventricular (**b**) craniopharyngiomas with the floor of the third ventricle (*dashed*)

attend a special education school, not because of intellectual capacity but mainly because of impaired relation with her classmates. There were no other mental disturbances precluding normal school education in the other survivors. Impaired cognitive function present before surgery in one patient improved after radical tumor removal.

Intraventricular craniopharyngioma

In one patient, the entire tumor was located inside the cavity of the third ventricle; its basal surface was covered by the third VF. The tumor which was exposed through the opening of the lamina terminalis was attached to the ventricular floor; a part of the latter was atrophied at the region of the infundibulum but the tumor was confined to the cavity of the ventricle. Blunt dissection disclosed the border and a plane of cleavage between the tumor capsule and the tuber. The attachment to the lateral walls was loose; the capsule could be easily detached. Nevertheless, a small tumor remnant was left in the posterior part of the third ventricle (Table 2). It was not exposed to direct view through the microscope; it could be seen only with an angled endoscope but could not be removed though the opening of the lamina terminalis below the AComA. Later on, the tumor remnant showed fast progression and was removed in 5 months via transcallosal approach. On day 7 after the first operation, left-sided hemiparesis with ischemic changes in the region of the right middle and anterior cerebral arteries occurred. Hemiparesis resolved completely later on. At the end of the follow-up, 102 months after surgery, the patient had diabetes insipidus and hypopituitarism except for corticotrophin activity; she developed obesity after the second operation. She has no visual or mental disturbances.

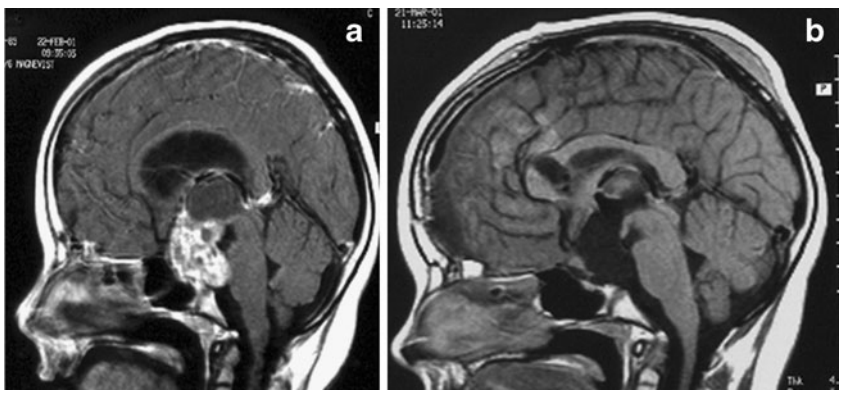

Fig. 5 Intraventricular and extraventricular craniopharyngioma (**a**) resected through one-stage combined transcallosal and subfrontal-trans-lamina terminalis approach (**b**)

Radiotherapy

Altogether, six children received eight courses of different types of radiation therapy. The patient irradiated initially after the radical removal of recurrent tumor had no recurrences afterwards. Out of five patients with incompletely removed recurrent tumors, three received one type of irradiation; in two others, two different types of treatment in different stages of the disease were administered, namely, radiosurgery and external radiotherapy (XRT) in one and XRT and brachytherapy with yttrium-90 in the other patient. Radiation precluded recurrence or progression altogether in three cases and was inefficient five times. After XRT, two tumors remained stable and three progressed. A solid tumor remained stable after radiosurgery; another cystic one progressed. The repeated instillation of Y90 into the tumor cysts in one patient was ineffective.

Discussion

An analysis of our pediatric series showed that the success of safe radical removal of craniopharyngioma depends on the topography of the tumor. The rate of morbidity and mortality was higher in IEVCs than in SEVCs or ISCs which are tumors located outside the third ventricle. In adult patients, this correlation was even more pronounced. Morbidity and mortality was correlated with the location of the tumor on the vertical pituitary–hypothalamic axis: the least in ISCs, higher in SEVCs, and the highest rate was observed in IEVCs.

Anatomical relationships relevant to the surgery of craniopharyngiomas

The safety of the radical removal of a craniopharyngioma is predetermined by its relationship with the meninges. Removal of ISCs, originally infradiaphragmatic tumors, is facilitated by the presence of arachnoid between the third VF and the membrane formed by the fibrous tumor capsule as well as by the distended sellar diaphragm. The capsule of SEVCs is in direct contact with the pia of the third VF. Firm adhesions between them precluding radical removal of the tumor capsule without damaging pial vascular network were found less frequently in children than in adults. Therefore, SEVCs could be safely radically removed even if they grew in posterior-superior direction against the floor of the third ventricle; severely compressed and displaced hypothalamic structures provided small branches of internal carotid and posterior communicating arteries are dissected free and spared [38]. The IEVCs come in direct contact with the diencephalic structures with no intervening leptomeningeal structures; their removal therefore is most complicated.

The policy of limited surgery in all cases of pediatric craniopharyngiomas followed by focused conformal radiotherapy in order to preserve the arachnoidal planes for subsequent surgery in children in whom the tumor relapses [1] thus cannot be supported by our morphological data and our clinical experience. There is no arachnoid plane between the majority of supradiaphragmatic craniopharyngiomas and the third VF. Even small craniopharyngioma may be embedded in the hypothalamus since the beginning of its origin [23].

We also cannot recommend intentional incomplete removal of all tumors "involving hypothalamus" [31] without defining the exact relationships of the tumor and the hypothalamic structures. Craniopharyngioma extending retrochiasmatically encroaching upon the third ventricle with "the hypothalamus no longer identifiable" [27] may only compress and not destroy the hypothalamus and may be safely radically dissected free. From a practical point of view, it is very important to distinguish between the SEVCs and the IEVCs. Retrochiasmatic position of a tumor is sometimes considered as an evidence of its intraventricular location [25]. However, in our morphological and clinical series, we have encountered not only SEVCs but occasionally also ISCs growing completely behind the optic chiasm. Preoperative MRI in patients with a large or a giant tumor does not enable a direct identification of the structures of the third VF; however, the position of the latter may be assumed indirectly. An important sign is the hydrocephalus which is common in the IEVCs and is extremely rare in an extraventricular tumor even if the later occludes almost the whole ventricular chamber [39]. Thinned out and stretched third VF in SECs and large ISCs have been seen occasionally through the microscope and in majority of the cases it could be seen only by means of the endoscope. The third VF was usually clearly displayed on postoperative MRI.

Even small IEVC with its upper pole below the foramina of Monro may cause enlargement of the lateral ventricles and the rest of the third ventricular chamber; however, in cases without hydrocephalus, it is often impossible to ascertain the relation of a small- or medium-sized retrochiasmatic tumor with the third VF before surgery. The defect of the third VF on postoperative MRI scans [25] is not evidenced. It may be interpreted as intraoperative hypothalamic damage [6, 27] and it may also be created by the tumor itself already before surgery as it has been shown by our morphological studies [37].

The extent and avidity of adherence of craniopharyngiomas extending into the third ventricular cavity to the remnants of the floor and the lateral walls of the ventricle may also vary significantly. According to the results of our morphological studies, the less severe the atrophy and displacement of the remnants of the third VF, the less

intimate is the adherence of the tumor to the lateral ventricular walls [37]. In rare cases of purely IVCs where the third VF was almost completely preserved, the tumor adhered only to the inner surface of the floor and only touched the lateral walls of the ventricle, but IEVCs adhere not only to the remnants of the floor but also to the lateral walls of the ventricle. This morphological observation, confirmed also in our clinical series, was later on reported by others [24, 47]. The upper pole of IEVCs at the region of the foramina of Monro usually only touches the walls of the ventricle and does not adhere to them. In this respect, the transcallosal approach is advantageous over the transla-mina terminalis route as the removal starts at this part of the tumor and proceeds basally where the tumor merges with the hypothalamus. The most problematic part of surgery of IEVCs is searching for the borders of the lateral parts of the tumor at the level of its "equator" where it adheres to the remnants of the tuber. Careful inspection may reveal the clear plane of cleavage between the gliotic tumor capsule and the hypothalamic structures. In some cases, a distinct capsule can be easily detached from a lateral wall and from the remnants of the third VF and the tumor may be removed radically; otherwise, a part of the capsule or even tumor tissue has to be left in place. If the plane of cleavage is not completely clear, even incomplete removal may lead to severe acute hypothalamic insufficiency which requires management by intensivists experienced in pediatric neurointensive care. Therefore, the final decision about the optimal extent of tumor resection has to be made at the operation.

Early and late outcome of surgery

Acute hypothalamic insufficiency necessitating pediatric neurointensive care occurred in our series after both radical and subtotal removal of some IEVCs. Any additional damage to the atrophied hypothalamus caused even by gentle surgical manipulation may be dangerous or even fatal. It was the cause of a single early postoperative death.

Long-term survival rate and the quality of life of the survivors in our series were different in different topographical groups of tumors. At the end of the follow-up, all patients with ISCs were alive, 80% of patients with SEVCs survived, and only 64.7% of patients with IEVCs/IVC survived. The cause of late mortality was either multiple tumor recurrence or chronic hypothalamic insufficiency and inadequate hormonal replacement. The later was observed in IEVCs during the early period of the series after both radical and incomplete tumor removal.

A great majority of patients needed both anterior and posterior pituitary hormonal replacement. The patients who did not need any anterior pituitary hormone replacement or who needed only partial substitution were most often encountered in the group of ISCs. They all had primary radical tumor removal. The same was true for diabetes insipidus. All eight patients surviving after subtotal or partial tumor removal required complete anterior pituitary hormone and antidiuretic hormone replacement. Preservation of the remnants of pituitary gland and the stalk did not always prevent hypopituitarism and diabetes insipidus. Complete regression of preoperative diabetes insipidus was observed in a single patient after the radical removal of an ISC.

Obesity was observed in almost two thirds of children with the tumors growing inside the cavity of the third ventricle, i.e., IEVCs and IVC. This may be in agreement with observation of worse outcome and lower quality of life in patients with retrochiasmatic craniopharyngiomas and with tumors causing hydrocephalus [5, 9, 26, 33, 47]. Obesity which occurs predominately in this topographic group may also result from the continued impact of preoperative hypothalamic damage [45]. Weight gain did not occur after primary removal of large and giant SECs that were severely compressing the hypothalamus.

Neuropsychological sequelae interfering with education were present in a single patient among all survivors in our series. A girl, after removal of an IEVC, had behavioral dysfunction and impaired relations with her classmates without impairment of intellectual abilities. This was observed also by others [25]. Severe mental disturbances gradually also evolved in another patient who died 8 years after removal of IEVC. There were no other postoperative mental or cognitive dysfunctions in the rest of the pediatric series. Preoperative memory impairment and behavioral problem in four patients (two ISCs, one SEVC, one IEVC) resolved after surgery.

Contrary to other functions, the visual outcome in patients with ISCs was relatively worse when compared to that with supradiaphragmatic craniopharyngiomas. Postoperative worsening of vision in the series of Di Rocco [8] was also observed most often in patients with craniopharyngiomas growing in front of the chiasm. The cause of this phenomenon may be a severe compression and strangulation of the structures of visual pathways between the tumor and the anterior cerebral arteries. This, however, does not explain the better results in our patients with SEVCs which partially grew in front of the chiasm. According to literature reports on craniopharyngiomas, visual functions remain stable after surgery in majority of the children. Postoperative improvement of vision was observed in 20.4–68%, while impairment was reported in 6.7–33% of the patients [3, 8, 11, 27, 43, 48]. The level of vision in our children was rather good; all but two could read at least by one eye. The postoperative worsening rate was close to the lowest rates reported in the literature. There was a difference between the pediatric and adult parts of our series; unlike in

the series of Fahlbusch et al. [10], postoperative visual worsening was more often observed in children. This is probably caused by neglecting the visual defects by pediatric patients. Surgical decompression cannot prevent the continuing atrophy of the anterior visual pathway and stabilize the visual functions severely worsened before surgery.

Tumor recurrence

The tumors primarily operated in our department were not irradiated before or after primary surgery and not before repeated surgery; they recurred in almost one third of the patients. It occurred in one eighth of the patients with ISCs, in a quarter of patients with SECs, and in approximately half with the IEVCs and IVC. In the series analyzed as a whole, the recurrence rate after primary surgery was higher after incomplete (42.8%) than after radical (30%) removal as reported also by others: Choux et al.—56.6% and 19.1% [3], Dhellemnes and Vinchon—93% and 43% [7], Di Rocco et al.—50% and 7% [8], Duff et al.—22% and 6% [9], Lin et al.—100% and 43% [20], and Sainte-Rose et al.—54% and 36% [31] after subtotal and after radical removal, respectively. Lena et al. [19] found no other prognostic factors among those studied (age, sex, location, aspect, size of the tumor, and result of the first MRI 3 months after surgery) concerning the recurrences of craniopharyngiomas except the quality of the exeresis as confirmed by the first postoperative MRI. However, this could not be verified inside the topographical groups of our series first of all because of a low proportion of incompletely removed extraventricular tumors. An observation deserving consideration is the extremely high recurrence rate after the radical removal of IEVCs. The explanation may be the presence of the microscopic outgrowths of tumor parenchyma into gliosis and even into normal brain tissue in the immediate vicinity of the tumor [12, 17, 23]. These are not visible through operative microscope and may remain in place after "radical" tumor removal if not detected by postoperative MRI scans.

Surgery of recurrent craniopharyngiomas is known to be more difficult than primary surgery and is followed by worse outcome [10, 18, 32, 33, 46]. According to our experience, early surgical removal of recurrent craniopharyngiomas may considerably help to solve these problems. Our policy was to remove the recurrent tumor as soon as it is detected. Similar to Rutka et al. [30], our intention is to achieve gross total resection of the lesion. Removal of a small tumor was easier and rarely caused any additional deficit. There was no mortality after 23 operations in 16 patients (four primarily operated elsewhere and 12 recurring after primary surgery in our department), and there was no other morbidity besides the partial unilateral worsening of vision in two patients. This is in agreement with the results of Minamida et al. [22] who safely managed recurrent craniopharyngiomas by using meticulous microsurgical techniques without additional radiotherapy.

Adjuvant radiotherapy

The efficacy of radiotherapy in the management of craniopharyngiomas, benign epithelial tumors, is documented in the literature. Even the superiority of radiotherapy alone, over combined surgical and radiation treatments, has been reported [15]. However, in majority of the series presented in related papers, radiotherapy is administered as an adjuvant therapy with a different rate of therapeutic effect. Decreased recurrences from 44% to 16% were observed after doses higher than 54 Gy [29]. The patients in our series in whom conventional XRT was ineffective received lower doses because they were treated also by other forms of irradiation. Choux et al. [3] reported a lowering of the rate of recurrences of incompletely removed craniopharyngiomas from 56.6% without irradiation to 29.6% after radiotherapy. Karavitaki et al. [16] observed an increase of the 10-year survival rate from 38% after partial tumor removal to 77% after partial removal plus irradiation. Lin et al. [20] stressed the necessity of initial radiotherapy after subtotal removal which is more efficient than irradiation administered at the time of the relapse. Still others found no relation between recurrence and adjuvant radiotherapy, neither globally nor in patients with incomplete resection [42]. In the series of Zuccaro [48], all children who underwent total removal without radiation therapy are able to go to a normal school, with a status of no more than a year behind the expected grade. Conversely, of the children who underwent subtotal removal with radiotherapy, only 62% were able to attend the level of education according to their age.

Such an inconsistence of the results of radiotherapy may be caused by the extremely variable biological behavior and unpredictable growth rate of craniopharyngiomas observed in our clinical and morphological series and by others [36]. Some craniopharyngiomas recurred within a year or two while others remain stable for years. Di Rocco et al. [8] observed that many residual craniopharyngiomas can remain stable at follow-up even without any adjuvant therapy. Therefore, they do not suggest any further treatment after surgery in case of non-progressive tumor to avoid complications, such as hypothalamic dysfunction or vascular damage. There were no adverse effects attributable directly to irradiation in our clinical series; however, we have observed an occlusion of the internal carotid artery after combined external radiotherapy and intracystic brachytherapy in a child in our morphological series. Hypothalamic damage caused by radiation therapy

occurred in two children in another of our clinical series, namely, with gliomas of the third ventricle. Therefore, our current policy is not to irradiate stable residual tumor. We reserve radiotherapy or radiosurgery for the progression of unresectable remnants of the tumor. Nevertheless, indication for radiotherapy should probably be reconsidered in the group of patients with IEVCs because of very high recurrence rate even after radical removal which was not comparable with the rest of our series of children and adults.

Conclusions

Long-term survival rate after primary craniopharyngioma surgery was higher after radical tumor removal (90%) than after incomplete excision (57.1%). There was a difference between the topographic groups which to some extent copied the rate of radical tumor removal. At the end of the follow-up, all patients with ISCs were alive; 80% of the patients with SEVCs survived and 64.7% of the patients with IEVCs and IVC survived.

The quality of life in patients with supradiaphragmatic tumors varied according to the relationships of the tumor with the floor of the third ventricle. Hypothalamic signs and symptoms were more frequent after surgery of IEVCs than in children with extraventricular craniopharyngiomas. There were no mental disorders or obesity caused by the primary removal of SEVCs including those severely compressing hypothalamus. The latter may be removed radically much more safely despite an apparent hypothalamus involvement. Therefore, it is important to distinguish between these two topographical features before surgery. The swing of the pendulum towards intentional incomplete removal of all retrochiasmatic tumors without knowing the true relationship of the tumor with the hypothalamus should be slowed down.

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