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Long-term results of treatment for craniopharyngioma in children

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Abstract Results of the treatment of 27 children with craniopharyngioma are reported. A subfrontal pterional approach was used in 55.6% of cases, a transsphenoidal and a transcallosal or transcortical approach in 25.9% and 18.5% of cases, respectively. Radical removal was the goal of surgery and was achieved in 70.8% of cases treated as primary surgery. The operative mortality was 3.7% and was due to hypothalamic failure. Most (81.4%) patients were followed up, for a mean of 7 years. Patients were evaluated according to a functional evaluation scale and outcome categories proposed by us. The scale takes account of tumor (recurrences and their eventual evolution); visual functions; endocrine functions (mainly hypothalamic), attainment of endocrine balance and drug regimen; headache; and psychosocial function. Recurrences were observed in 17.6% of patients treated with radical surgery and in 42.8% of those treated with limited surgery plus radiotherapy. A progressive amelioration of visual, endocrine and neuropsychosocial functions from the intervention to follow-up was observed in the majority of patients. Complete tumor excision was associated in 85% of cases with a low score on the functional scale, reflecting a high functional performance. Adequate substitution therapy maintained endocrine balance in 81% of patients. Since the intervention a progressive decrease in the number and dosages of medications has been observed. The majority of patients were again able to lead a normal social life. Small stature, obesity, headache, and emotional and sexual disturbances were frequent cause of long-term disability even despite adequate drug regimens. The functional evaluation scale we propose is a simple and effective tool that can be easily used during routine evaluation of patients with craniopharyngioma.

Key words Craniopharyngioma · Radical surgery · Outcome · Evaluation scale · Children

Introduction

The ideal goal of treatment for craniopharyngiomas should be complete tumor removal with improvement of altered visual functions and minimal deterioration of endocrine functions without neuropsychological and social deficits. However, these results have not been achieved in all cases, particularly in the pediatric age group. Even though mortality has been substantially reduced in recent years, radical surgery has been criticized, particularly because of the occurrence of a considerable number of cases of postoperative panhypopituitarism requiring hormonal substitution therapy [12, 13, 19, 26, 31, 32, 47, 48]. Controversies about quality of life and the occurrence of neuropsychological disturbances are also reported [6, 7, 11–13, 34, 43]. In con-

trast, psychological and endocrinological side effects are described by some authors in pediatric patients after irradiation following subtotal or partial resection [11, 30, 43, 50, 51]. The incidence of recurrences after radical surgery and subtotal removal followed by radiotherapy is another issue under debate [7, 15, 18, 34, 43, 50, 51]. The most appropriate treatment modality must provide the longest tumor control and the lowest morbidity [7, 15, 17, 18, 43, 50, 51]. What constitutes acceptable morbidity has to be evaluated in term of quality of life, but how to assess the quality of life is one of the most difficult issues. The problem is compounded by several factors. Various studies in the literature have been focused on single factors, with sophisticated methods proposed for their evaluation [6, 29, 36]. We started out from a more practical demand. Our requirement was for a simple instrument allowing quick, easy, and at the same time accurate evaluation of any patient harboring a craniopharyngioma, at every step of his or her clinical history. The tool should include most of the variables usually recognized as those determining the quality of life. So far we have designed a functional evaluation scale comprised of different parameters; we believe this scale would be useful for the evaluation of quality of life of patients with craniopharyngioma.

The aims of this work were: to report the surgical and long-term results in our series of patients treated for craniopharyngioma; and to verify the usefulness of administration of the functional scale to our series of patients.

Patients and methods

Patients

Between 1977 and 1994, 27 children with craniopharyngioma were admitted for treatment at our Institution. The age at diagnosis ranged from 6 to 16 years, with a mean of 11 years. All patients, except the earliest (4 patients), who were studied with plain skull X rays, polytomography and angiography, were evaluated with sagittal and coronal CT scans and, more recently, with CT and MR imaging. Many of them (40.7%) also had preoperative angiography, although more recently information obtained by MR had been considered sufficient and angiography is now no longer performed. Endocrinological, ophthalmological and neurological examinations were performed before surgery.

As we reported in our previous work [44], our policy was the surgical treatment of the tumor with an attempt at radical removal whenever possible. The rational of the surgical philosophy, the choice of the surgical approaches and the cases in which a shunt was implanted are described in our previous report [44].

Presenting features

Visual disturbances, headaches and endocrine disorders were the most common presenting symptoms. Visual disturbances were documented in 16 patients (60%), all of whom had decreased visual acuity; 11 (40%) also had visual field deficit. Headache was present in 57% of patients (15 cases). The duration of headache before diagnosis was 2 years on average. Sixteen patients (60%) were found to have endocrine disturbances. Stunted growth was evident in 18 patients (68%), and amenorrhea and obesity each in 6 patients (23%). Diabetes insipidus was diagnosed in 7 patients (27%). Most of these symptoms developed progressively. In 3 patients (10%) the onset was relatively acute.

Only 2 patients (8%) had psychic disturbances and/or cognitive deficits.

At diagnosis, ventricular enlargement was noted on CT in 50% of patients. Signs and symptoms of intracranial hypertension were present in 9 patients (33%).

Tumor location and size were classified as previously reported in the literature [50, 51]. In 2 cases (7.4%) the tumors were intrasellar, while 13 (48.2%) were intrasuprasellar, 7 (25.9%) suprasellar extraventricular, and in 4 cases (14.8%) an intra-/extra-ventricular location was noted. In 3.7% of cases (1 patient) the tumor was purely intraventricular. In 33.3% of tumors (9 cases) the size was classified as small (<2 cm), in 44.4% (12 cases), as medium (2–4 cm) and in 22.3% of cases (6 cases), as large (>4 cm).

Treatment

Twenty-four patients had their first surgery for craniopharyngioma at our Institution, while 3 patients were operated on at our Institution for a symptomatic recurrence of a craniopharyngioma initially treated elsewhere.

In 7 patients (25.9%) tumors were removed by a transsphenoidal approach. Of the remaining 20 patients, 15 (55.6%) were treated via a subfrontal pteryonal approach and 5 (18.5%), via a transcallosal or transcortical approach. A combined transcallosal plus subfrontal pteryonal approach was used in 2 patients (7.4%). In these cases two separate procedures were used, with complete recovery from the first procedure before the second was initiated.

The extent of radical resection was assessed on the basis of postoperative contrast CT according to the scale established by Hoffman et al. [16]. Removal was considered to be total when the postoperative CT scan showed no evidence of residual tumor (grade 1) or of even a tiny calcific fleck without evidence of enhancement or mass effect (grade 2). In all other cases (from grade 3 to grade 5) the extent of resection was estimated to be limited. Additional postoperative MR was used to confirm the extent of surgical resection of the tumor achieved.

Operative mortality was defined as death occurring within 30 days of surgery. Long-term deaths were characterized as being either secondary to tumor progression or from other causes. The details of adjuvant treatments for the patients who received postoperative radiation therapy were also recorded. During the period under scrutiny and, especially, in the earlier cases in this series, conventional external radiotherapy was performed. The usual total dose was 50–55 Gy. The radiosurgical option (gamma knife) has been available to us for the last 2 years.

Histology

Histology revealed an adamantinous subtype in most of the tumors (80%) and a mixed one in the rest. Microscopic evidence of calcifications, cholesterol clefts and keratin nodule formation was also noted.

Follow-up

Twenty-four patients were available for follow-up. Follow-up ranged between 2 and 19 years (mean 7 years). Data were obtained from 22 patients (91.6% and 81.4% of the overall number).

Follow-up involved a written questionnaire, telephone inquiry, direct examinations, scheduled CT and MR examinations, and endocrinological and ophthamological examinations. The questions in

the written questionnaire dealt with general mood, education, changement and type of work, hormonal substitution therapy, stature, weight, presence of sexual disturbances, diabetes insipidus, amenorrhea, and more recent endocrinological, ophthamological and neuroradiological examinations. Patients were also asked to give a direct judgment of how they felt and their level of performance.

Specialist endocrinological and ophthalmological examinations were performed during direct examinations. Particular attention was paid to hormone substitution therapy (drug regimen), particularly the number of medications and their dosage. Direct observation of behavior, reports from parents and teachers, details of educational placement level of social reintegration and aid in the assessment of neuropsychological functions were considered.

Evaluation scale and follow-up categories

Evaluation of the long-term results of patients treated for craniopharyngiomas should take account of the persistence of tumor remnants and their possible regrowth, the visual and endocrine functions with particular attention, in the pediatrics group, to obesity, growth deficits and sexual disturbances. School education deficits together with the ability to initiate or to maintain working activities and the general mood are other parameters to be evaluated. From these standpoints, we designed a functional evaluation scale embracing all the parameters previously reported (Table 1). Each parameter had a different score according to its specific clinical relevance. The score ranged between 0 (minimum score) and 15 (maximum score). Three different score groups were identified: from 0 to 5 (good), from 6 to 10 (moderate) and over 10 (poor). These groups were related to subjective evaluation scores given directly by the patients at follow-up according to how they felt and their subjective level of performance.

Moreover, patients were classified according to various outcome categories. These categories were created to take account of the presence/absence of tumor remnants or regrowth, attainment (or not) of endocrine balance, features of drug regimens, emotional status. Five categories were considered: A Complete cure: patients without tumor recurrence and with endocrine balance controlled without drugs; B patients without tumor and with endocrine balance controlled with drugs; C patients without tumor and with endocrine balance not controlled even with drugs; D patients in whom a tumor remnant was demonstrated on MR and who had endocrine balance controlled with drugs; E patients in whom a tumor remnant was demonstrated on MR and endocrine balance was not controlled even with drugs.

Table 1 Functional evaluation scale

Tumor		Headache	
No tumor	0	No	0
Remnants, stable	2	Yes	1
Regrowth	4	Working ability	
Visual functions		Normal	0
Improved	0	Yes, reduced	2
Unchanged	1	No	4
Worsened	3	Mood disorders	
Endocrine functions		No	0
No drugs	0	Yes	1
Drugs, balanced	1	Sexual disturbances	
Drugs, unbalanced	3	No	0
Diabetes insipidus		Yes	1
No	0	Stature deficits	
Yes	1	No	0
Obesity		Yes	1
No	0		
Yes	1		

Results

Surgical treatments

Radical removal was the goal of surgery in all cases. This was achieved in 17 patients (70.8%) out of 24 undergoing primary surgery. There is a direct relationship between radicality and tumor dimension. Radicality was obtained in 86.7% of tumors classified as small, in 65.5% of those considered as medium sized, and in 38.4% of large tumors. In all these tumors the presence of a distinct plane of cleavage between the tumor and the surrounding neural tissue allowed safe dissection from the region of the floor of the III ventricle. Opening of the lamina terminalis allowed removal of the retrochiasmatic portion of the craniopharyngioma.

Limited surgery was performed on 7 (29.1%) of the patients undergoing primary surgery. Most of these harbored medium (58.9%) or large (5.8%) tumors. The reasons for the unsuccessful total resection were dense adherence of a portion of tumor capsule, to the optic chiasm in 3 patients (all cases prefixed) and to the carotid artery in 2 cases. In the remaining cases, the presence of severe hypothalamic adhesions made radical resection too hazardous.

The tumor was adherent to the carotid and its major branches in 8 patients, to the hypothalamus in 10 patients and to both in 3 patients.

In 4 of the patients in whom only limited surgery was performed, the treatment was complemented with external radiotherapy started shortly after surgery. The remaining 3 patients were subjected to scheduled-clinico radiological follow-up because of the presence of small asymptomatic remnants.

In the group of patients undergoing secondary surgery, partial resection was achieved in 2 patients.

Among 27 patients operated on there were 3 intraoperative complications (11%). In 1 case severe brain edema developed suddenly after the dura was opened and the frontal lobe retracted. In another, damage to the middle cerebral artery occurred during dissection of the tumor. Damage to the undersurface of the right frontal lobe occurred in the remaining patient. No bleeding or damage to the carotid artery or significant profuse venous bleeding was registered. There was 1 operative death attributable to dramatic postoperative hypothalamic failure (3.7%). No cases of operative mortality have been recorded since 1982.

In 1 patient a postoperative shunt was implanted because hydrocephalus developed. Only 1 patient needed an initial procedure for relief of hydrocephalus.

The pituitary stalk was identified in 50% of cases and preserved in only 30%. It was sectioned and removed in the presence of tumor infiltration, to avoid recurrences.

Results of surgery

Visual functions

Among 16 patients with preoperative visual deficits, only 1 of 3 patients with severe visual impairment improved postoperatively, whereas 1 patient maintained a stable deficit and the the other developed a monocular amaurosis.

Out of 13 patients with mild or moderate preoperative visual deficits, 8 patients (61.5%) maintained stable deficits and the others (38.5%) improved slightly. Overall, in 10 patients (37.1%) visual acuity improved, 5 patients (18.5%) had a deterioration and 12 patients (44.4%) remained stable. Postoperative hemianopsia was noted in 5 patients.

Endocrine functions

Postoperative endocrinological deficits were noted in the great majority of cases. Postoperative diabetes insipidus (DI) was present in 22 patients (81.4%). DI was transient in 4 patients (18.1%). Most patients developed DI after 2 or 3 days of surgery. A hormonal substitution polytherapy was administered to most patients.

Neurological functions

No major motor disorders were observed. One patients had moderate hemiparesis. At discharge all but 1 of the patients returned home and were able to care for themselves.

Recurrences

In the group of 17 patients in whom radical removal was achieved, 3 recurrences were documented (17.6%). One patient with a symptomatic recurrence underwent secondary surgery, which was considered radical. Another patient with a small recurrence was submitted to conventional radiotherapy. The last patient had a small asymptomatic recurrence without evidence of further regrowth at MR follow-up examinations.

The child who underwent reoperation died after 3 years of progressive deterioration of the neurological condition and endocrine failure.

In the group of 7 patients who had only limited surgery, 3 had remnants that regrew (42.8%). Two patients with symptomatic recurrences underwent radical re-operations. One patient with a small recurrence received radiotherapy, and so far no evidence of further regrowth has been documented.

Recurrences occurred during the first 3 years after treatment.

Follow-up

Only patients subjected to primary surgery were followed up. Out of 24 patients, data were obtained from 22 (91.6%). Progressive amelioration of visual, endocrine and neuropsychological functions was noted in the majority of patients.

Visual functions

Although 3 patients had severe postoperative visual impairment, those with mild or moderate postoperative deficits showed progressive improvement of visual acuity that allowed resumption of their social and working life. There were 9 patients who improved to 9/10 and 2 patients, to 10/10; the rest improved to 7/10. In spite of amelioration of the visual acuity, in none of these children did the visual fields significantly improve.

Endocrinological functions

Most patients had anterior and posterior pituitary deficiency which did not differ according as whether or not complete removal had been achieved (Table 2). Management with hormone replacement was not particularly difficult. Adequate hormone substitution maintained the endocrine balance in most patients. Since the interventions a progressive decrease in the number and dosage of medications has been observed (Table 3).

Out of 15 patients in whom a radical removal was attained, only 2 had endocrine dysbalance requiring high-dose medications and continued adjustments of their drug regimens. All the rest reached endocrine balance with a low-dose regimen (Tables 2, 3).

All patients with limited surgery reached endocrine balance. All but 1 required replacement therapy with a low-dose drug regimen. In the others endocrine balance was reached with a high-dose drug regimen that required continuous adjustments (Tables 2, 3).

Table 2 Deficits at follow-up

Psychosocial disturbances		59%
Headache		63.6%
Obesity		
Frank (>25%)	41.0%	77.3%
Mild	36.3%	
Sexual disturbances		
Uncontrolled	14.0%	41.0%
Controlled	27.0%	
Diabetes insipidus		50%
Small stature		59.4%

Table 3 Drug regimens in patients with controlled vs uncontrolled endocrine balance

	Low (%)	High (%)
Cortisol (2–3 mg/kg/day)	75.0	25.0
DDVAP (5–10 Y/day X 2)	66.6	33.4
Thyroxine (4–10 µg/kg/day)	72.7	27.3
Estradiol, FSH, Testosterone	66.6	33.4

Nothwithstanding these positive results, obesity, small stature and sexual disturbances were frequent causes of long-term disability (Table 2).

Obesity was present in 17 patients (77.3%). Frank obesity was observed in 41% of the children, developing in cases with significant hypothalamic involvement. No differences were observed between patients with radical and with limited removal. The management of obesity in this group of patients was particularly difficult.

Small stature was reported in 59% of patients, with no difference between patients treated with radical and with limited surgery.

Sexual disturbances (loss of libido and impotence) were recorded in 41% of cases; most of the patients complained of mild disturbances, which were frequently sporadic. Severe or stable disturbances were noted in 27% of patients requiring high-dose regimens and continuous adjustments of their medications. These disturbances were more frequently seen in male than in female patients (65% vs 35%).

Psychological and social functions

The majority of patients were able to resume a normal social life and become reintegrated. Except for 3 patients with severe visual and endocrinological deficits, in whom quality of life was severely impaired, none of the patients had any major changes in their social and academic performance. Four of them had university degrees, 8 had high school degrees, and the rest attended normal educational establishments. In the last group, 6 had jobs and were able to pursue them. The others were temporarily unemployed. No significant changes in short- or long-term memory functions were observed in these groups of patients.

Mild emotional changes were complained of by 59% of patients and were characterized by emotional shifts from aggressive to labile/apathetic affect (Table 2). Many patients were distraught over body image changes as a result of excessive weight gain following diagnosis and treatment. Such disturbances were more common among female than male patients (67.5% vs 32.5%).

Recurrences and remnants

At follow-up 2 patients in the group treated with radical surgery and 2 patients treated with limited surgery had tumor remnants. In all these cases tumor remnants appeared as stable at the latest neuroradiological controls.

Functional evaluation score and patients' subjective evaluation

In the group of 15 patients in whom a radical removal was achieved (Table 4), 12 patients (85.7%) had scores ranging from 0 to 5 and 2 patients (14.3%), scores between 6 and 10. Eleven patients (78.6%) felt they were functioning well and 3 (21.4%), moderately well. A strict relationship between the score on the evaluation scale and each patient's subjective evaluation was noted.

In the group of patients treated with limited surgery (Table 6), 4 patients (66.6%) had scores between 0 and 5 and 2 (33.4%), scores between 6 and 10. In this group, 83.3% of patients judged their own result as good and 16.7%, as moderate.

Outcome categories

In the group of patients with radical removal (Table 5), none could be considered cured (no tumor and endocrine

Table 4 Children subjected to radical surgery. Functional evaluation scale and patients' own subjective evaluation

Functional evaluation scale score			Patients' subjective evaluation		
Score	No of patients	%	Evaluation	No. of patients	%
0–5	12	85.7	Good	11	78.6
6–10	2	14.3	Moderate	3	21.4
> 10	–	–	Poor	–	–

Table 5 Children subjected to radical surgery. Classification according to outcome categories (B+C=85.8%)

Outcome categories		No of patients	%
A	Complete cure	0	0
B	No tumor, endocrine balance controlled with drugs	10	71.5
C	No tumor, endocrine balance not controlled with drugs	1	7.1
D	Remnants, endocrine balance controlled with drugs	2	14.3
E	Remnants, endocrine balance not controlled with drugs	1	7.1

Table 6 Children subjected to limited surgery plus radiotherapy. Functional evaluation scale and patients' subjective evaluation

Functional evaluation scale score			Patients' subjective evaluation		
Score	No. of patients	%	Evaluation	No. of patients	%
0–5	4	66.6	Good	5	83.3
6–10	2	33.4	Moderate	1	16.7
> 10	–	–	Poor	–	–

Table 7 Children subjected to limited surgery. Classification according to outcome categories

Outcome categories		No. of patients	%
A	Complete cure	0	0
B	No tumor, endocrine balance controlled with drugs	0	0
C	No tumor, endocrine balance not controlled with drugs	0	0
D	Remnants, endocrine balance controlled with drugs	4	66.6
E	Remnants, endocrine balance not controlled with drugs	2	33.4

balance with drugs; category A). Most of them (71.5%) were classified in outcome category B. Two patients still had two stable remnants and reached endocrine balance (outcome category D). One patient alone even without tumor remnant, was endocrine unbalanced. The sum of the percentage of patients classified as B and D well corresponds to that observed using the functional evaluation scale.

In the group of patients in whom only a subtotal or partial removal had been achieved (Table 7), no patient can be considered as cured. Most patients can be classified as B (66.6% of cases) and D (33.4% of cases).

Discussion

The treatment of craniopharyngiomas, particularly in children, is still difficult and controversial. Different treatment strategies have been proposed according to a multimodality plan [1, 30, 33, 50, 51]. All treatment plans considered should be evaluated in terms of both mortality, including long-term mortality, and morbidity. The most appropriate treatment modality should provide the longest tumor control and the lowest morbidity [11, 15, 18, 33, 43, 50, 51]. Various parameters have to be considered: age of the patient, clinical and neurological status, location, volume and extension of the tumor, presence of cysts and calcifications, experience of the surgeon, accessibility to radiotherapy and alternative treatments [11, 15, 33, 50].

Notwithstanding the various treatment options that have been recently proposed by many authors, we believe that microsurgery remains the mainstay of management of craniopharyngioma, even in childhood [1, 5, 20, 21, 22, 24, 26, 30, 45, 47]. Nowadays there are many controversies about the best surgical philosophy [7, 11–13, 15, 18, 31–33, 41, 43, 50, 51]. Radical removal has been frequently set against partial removal plus radiotherapy. We believe that radical removal should be accomplished whenever possible.

Nevertheless, radical removal cannot be achieved in all cases. We obtained radical removal in 70% of our cases. Various percentages have been reported in the literature [2, 4, 7, 11, 12, 13, 15, 18, 23, 25, 27, 33, 34, 40, 41, 43, 50, 51].

The feasibility of radical removal depends mainly on tumor size and extension [11, 46, 50, 51]. This relationship is well evidenced by our series (86.7% of radical removal in tumors classified as small vs 38.4% in those classified as large) and in the literature [11, 46, 50, 51]. In spite of advances and wider accessibility of neuroradiological examinations, craniopharyngiomas in childhood are large or medium-sized tumors by the time they are discovered [43, 46, 50, 51]. The large size influences the symptoms seen on admission [4, 7, 10, 11, 13, 18, 27, 34, 37, 41, 43, 46, 51]. In our series, most patients had visual and endocrine disturbances. Moreover, signs and symptoms of intracranial hypertension were of clinical relevance (33% in our series). It is therefore important to provide family doctors and pediatricians with information so that the preoperative diagnosis can be made earlier and surgeons can deal with small tumors.

When we plan a radical resection we should be aware that an attempt at absolute radicality could cause hypothalamic injury, major vessel damage, frontal lobe injury and/or injury to the visual pathways [11, 15, 18, 39, 46, 50, 51]. The level of these risks depends mainly on tumor location and extension.

In our series, craniopharyngiomas were adherent to the carotid artery and its major vessels in 8 cases (33.3%). In 1 case damage to the middle cerebral artery occurred during the dissection because of dense tumor adhersion to the vessels. A relationship between tumor adhersion and tumor size is reported in the literature [43, 46, 50, 51].

Many controversies concern the best surgical strategies when the tumor involves the hypothalamus [11, 15, 18, 34, 38, 43, 46, 50, 51]. Symptoms of hypothalamic disturbances are frequently present at diagnosis (68% in our series), and extensive tumor compression of the hypothalamus by the tumor seen on MR (evidenced in 40% of cases in our series) are prognostic factors of major hypothalamic involvement and consequently of postoperative hypothalamic morbidity [9, 11, 15, 18, 46, 50, 51]. The association between the so-called brain invasion and the extent to

which radical removal could be achieved is striking [7, 11, 15, 34, 46, 50]. Against this backdrop, we believe that the presence of a densely gliotic brain parenchyma surrounding the tumor capsule provides a margin of safety between the neoplasm and the hypothalamus. In our series this distinct cleavage was present in 68% of cases and allowed safe and radical dissection of the tumor from the floor of the III ventricle without resultant impairment of hypothalamic function. With regard to hypothalamic function no difference was observed between patients treated with limited surgery and radical removal in which that resection had been performed [11, 15].

Calcifications, seen in 68% of cases in our series, are typical of adamantinous subtype (evidenced in 96% of cases in our series) and may influence tumor resectability [8, 11, 28, 46]. Calcifications are located within the tumor capsule and adhere to neural and vessels structures; they can make resection too hazardous in some cases.

The adhesion of the tumor to optic nerves and chiasm has a significant influence on resectability and postoperative deficits [7, 11, 13, 15, 18, 27, 29, 46, 50]. In our series the tumor was densely adherent to the optic chiasm in 3 patients, precluding radical removal in all 3. When the optic nerves and chiasm are badly distended and stretched by the tumor they should be carefully manipulated. In such circumstances, significant deterioration of postoperative visual acuity, to the point of blindness, can occur (2 cases in our series) [29]. In our experience, the poorer the preoperative visual acuity, the higher is the incidence of postoperative visual deterioration. In these cases a limited surgical excision could lower the pressure on the optic tract, improve or normalize the vascularity, and lead to visual improvement that could finally allow safer tumor removal [29]. In the case of largely cystic tumors this could be accomplished by repeated cyst aspiration [1, 7, 21, 22, 24].

Preoperative signs of severe hypothalamic disturbances, young age at presentation, large tumor size with extensive tumor compression of the hypothalamus, severe hydrocephalus seen on MR, and intraoperative complications were predictive of high morbidity after the initial surgery and at long-term follow-up [11].

Operative mortality is still present (3.7% in our series), and it is mainly due to hypothalamic injury [7, 11, 15, 46, 50, 51]. Nevertheless, a trend toward zero mortality has been reached, particularly for those patients operated on with limited surgery [43, 46, 51]. In our series, no cases of operative mortality have been recorded since 1982.

Published series document excellent and equivalent clinical results and long-term survival following both radical surgery and limited surgery followed by radiotherapy [34]. What could differentiate these two treatment modalities is the rate of recurrence. A recurrence may be expected in 20% of patients on average after radical surgery and in 30% of the patients treated with limited surgery plus radiotherapy [7, 11, 13, 15, 18, 27, 30–34, 41, 43, 46, 49–51]. Moreover, a trend toward zero recurrences following total resection has been observed in the most recent neurosurgical series [43, 46, 50, 51]. Contrary to earlier belief, histopathological findings and brain invasion have no significant effect on recurrence [11, 46].

When there is a suspicion of regrowth we can perform revision surgery soon after the first operation or we can wait and carry out scheduled neuroradiological monitoring. In the first case, various strategies can be chosen. Secondary surgery has been recommended if gross tumor removal sems possible, particularly for solid components [7, 11, 43, 46, 50, 51]. Three patients (50%) in our series underwent reoperation. A radical removal is less frequently possible (40% in our series), and a worse clinical result and a higher incidence of sepsis are frequently reported. Greater difficulty of dissection is encountered, particularly in cases subjected to other treatment [11, 50, 51]. Radiotherapy can salvage approximately 80% of patients with recurrences [34, 42]. We administered radiotherapy to 2 patients (30%) with small recurrences. The complications of this treatment must not be overlooked [34, 45, 47, 48]. The effectiveness of alternative treatment modalities, such as stereotactic drainage of cysts, perhaps associated with intracavitary irradiation or intratumor instillation of bleomycin, have been well described in the literature [1, 5, 7, 21, 22, 24, 30, 35]. Recent reports suggest that radiosurgery is useful for the treatment of solid nests of tumor [21, 30].

In such cases, accepting that radical surgical removal could be deferred and performing effective alternative treatments may help to preserve quality of life and prolong survival of those patients in whom the results of clinical and radiological examinations at presentation are predictive of high morbidity and considerable mortality [11, 13, 43, 46, 47, 50, 51].

The most difficult issue to assess from the literature is quality of life [6, 11, 43, 46]. Usually surgical results are reported in term of good, moderate and poor outcome. We believe that any attempt to evaluate the quality of life should take account of different factors, mainly: recurrences, number of procedures, length of stay in hospital, disease-free period, visual function, endocrine function – mainly hypothalamic – and psychosocial function.

The functional evaluation scale we have proposed embraces various parameters: (1) tumor, presence of recurrence and development; (2) visual function; (3) endocrine function, mainly the presence or absence of diabetes insipidus, obesity, sexual disturbances, stature, but also drug consumption and the attainment of endocrine balance; (4) headache; (5) psychosocial functions, analyzed by studying the general mood of the patient according to the presence or absence of disorders of affect, and the ability to follow a normal education and to find and keep a job. For obvious reasons of simplicity, our analysis does not require the administration of complex neuropsychological tests.

The choice of these parameters, among the wide number of those available, rose from observations of which of

them significantly affected the quality of life of a patient with craniopharyngioma.

At follow-up, most patients in our series complained of headache (64% of cases), hypothalamic disturbances (obesity, small stature and diabetes insipidus in different percentages) and psychosocial disturbances (59% of cases). Most patients required hormone substitution therapy, which was able to maintain endocrine balance in most of patients (81.8% of cases). The number and dosage of medications (drug regimens) and the need for continuous adjustments were other factors affecting quality of life in terms of disease-free time. Quality of life was also influenced by the presence of recurrences and their evolution and further treatments. Accordingly, for each parameter of the scale a different numeric weighting is attached on the basis of its specific clinical relevance.

We did not have any difficulty in administering the scale to the patients. Patients could be easily and speedily studied at any stage in the follow-up, and also retrospectively. The reliability of this method is further confirmed by the existence of a good correlation among the score reported on the functional scale, the patients' subjective evaluation, and the various outcome categories we identified by grouping the different parameters previously reported.

Looking at the overall results of the series, only limited conclusions can be derived in view of the sizes of the samples. They are tempered by the limitations of all retrospective studies.

In all cases the primary goal was complete excision of the craniopharyngioma when it could be accomplished without significant mortality and morbidity (mainly visual and hypothalamic). It was feasible in 70% of patients on average, and in 85% of cases it was associated with a low score on the functional scale, the expression of an high functional performance. Limited removal was preferred in the case of giant tumors, in cases with a large retrochiasmatic extension, and in any case with dense adhesions to hypothalamus, vessels and visual pathways. A partial tumor removal was followed by radiotherapy. Limited surgery plus radiotherapy afforded a good quality of life and long-term tumor control in more than 70% of patients. Recurrences have been reported in 18% of cases on average. Most recurrences occur during the first 3 years after treatment. The rate of growth of tumor remnants is unpredictable. We reoperated in all cases of symptomatic recurrence. Small recurrences were submitted to radiotherapy or to scheduled neuroradiological monitoring according to individual conditions. At follow-up most patients had an improved level of visual function allowing their social and working reintegration. Adequate hormonal supplements had maintained the endocrine balance in 81% of cases, and regular pharmacological adjustments were necessary only in a small percentage of cases. Since the interventions, a progressive decrease in the number and dosage of medications has been observed. Small stature, obesity, headache, and emotional and sexual disturbances were frequent causes of long-term disability notwithstanding adequate drug regimens. The majority of patients resumed normal social life and very fully reintegrated.

The functional evaluation scale we proposed is a simple and effective tool that can be easily used by a neurosurgeon during routine follow-ups and studies. In any case the treatment of patients with craniopharyngioma must be individually planned and a multidisclipinary approach must be used in a attempt to provide long-term tumor control with the lowest possible morbidity [11, 15, 18, 43, 46, 50, 51].

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