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**M. Caldarelli**
**L. Massimi**
**G. Tamburrini**
**M. Cappa**
**C. Di Rocco**

# Long-term results of the surgical treatment of craniopharyngioma: the experience at the Policlinico Gemelli, Catholic University, Rome

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M. Caldarelli · L. Massimi ·
G. Tamburrini · C. Di Rocco
Section of Pediatric Neurosurgery,
Institute of Neurosurgery,
Catholic University Medical School,
Rome, Italy

M. Caldarelli (✉)
Istituto di Neurochirurgia,
Università Cattolica del Sacro Cuore,
Largo A. Gemelli 8,
00168 Rome, Italy
e-mail: mcaldarelli@rm.unicatt.it
Tel.: +39-063-0154587

M. Cappa
Department of Endocrinology,
Pediatric Hospital "Bambino Gesù",
Rome, Italy

**Abstract** *Background:* Craniopharyngioma (CP) is the most common intracranial non-glial tumour observed in pediatric age. Although histologically benign and amenable to surgical treatment, its location and relation with vital nervous and vascular structures makes the feasibility of a radical resection difficult even in the microneurosurgery era. Beside the difficulties experienced when performing tumour resection, post-operative complications, such as endocrinological imbalance, represent another point that makes CP total excision a challenge. In order to avoid such complications, some authors have suggested to renounce to radical resection and to rely on post-operative radiation therapy to minimise the risk of residual tumour progression.
*Methods:* We report our experience with 52 children and adolescents operated on for CP at the Department of Pediatrics, Section of Pediatric Neurosurgery, Catholic University Medical School, Rome, between January 1985 and December 2002. The study included 14 children <5 years old (five less than 2 years of age), 25 between 6 and 10 years old, and 13 more than 10 years old. The most common presenting signs were related to endocrinological imbalance (35 cases), increased intracranial pressure (32 cases), and to a lesser extent, visual compromise (17 cases). Concerning location, CP was intrasellar in three cases; sellar/suprasellar with prominent prechiasmatic growth in 24 cases; retrochiasmatic/3rd ventricular in 14 cases, and giant (with an extension into the middle and/or posterior cranial fossae) in 11 cases. The tumour was managed by means of a single surgical approach in 47 cases and with a two-stage operation in the remaining five cases. In 11 cases of intrasellar or intra/suprasellar midline location, the first surgical approach was done through the transsphenoidal route (which represented the first step of a staged operation in five instances); in the remaining 41 patients, craniotomy was the first surgical procedure. Radical tumour resection was achieved in 40 cases, subtotal (only small tumour remnants adherent to the carotid arteries, 3rd ventricle floor or visual pathways) in nine, and only partial in the remaining three cases
*Results:* Histology demonstrated the adamantinous variant in all cases. Two surgical deaths were recorded in this series (both following a transsphenoidal approach): one secondary to uncontrollable intra-operative bleeding from the carotid artery, and the other to fulminating bacterial meningoencephalitis. Morbidity included endocrinological disturbances, namely hypopituitarism and diabetes insipidus, in more than 80% of cases, worsening of pre-operative visual deficit in six cases, and transitory neurological deficits in five cases. One late death was recorded 2 years

after surgery, secondary to electrolytic imbalance although favoured by a major head trauma with subacute subdural haematoma. Nine recurrences occurred 1–8 years after surgery (three true recurrences, and six re-growths of incompletely resected tumours) that required re-operation. Twelve patients underwent radiotherapy, six after an initially incomplete tumour resection and six following relapse. One patient presented with a malignant thalamic glioma 8 years after radiotherapy. At long-term follow-up, all survivors showed good clinical condition, even though approximately 60% relied on hormone replacement, and some patients presented obesity. Diabetes insipidus has subsided in about 80% of the cases; visual deficits improved or remained stable, whereas post-operative neurological deficits subsided in all but one patient. *Conclusion:* In our experience, radical resection of CP represented the first and almost unique treatment modality. Although not insignificant, post-operative mortality and morbidity do not seem to represent a major contraindication in attempting a radical tumour resection whenever possible. On the other hand, extensive hypothalamic involvement should suggest a less aggressive attitude.

**Keywords** Craniopharyngioma · Radical resection · Recurrence · Post-operative complications

## Introduction

Craniopharyngioma (CP) is one of the most challenging central nervous system tumours for a neurosurgeon [3, 4, 17, 33]. The strict relationship of this tumour with the neighbouring cerebrovascular structures makes the surgical management of this tumour particularly risky for visual and endocrine functions, apart from the risks of injuring the major vascular trunks providing blood to the brain. The main target for the treatment of a benign tumour should be its radical removal whenever possible, to minimise the risk of tumour recurrence. Such a goal should be accomplished without or only with minimal functional impairment. Nowadays, sophisticated microsurgical techniques coupled with neurosurgeon's skillfulness have greatly reduced the surgical risk of injuring the nervous and vascular structures surrounding the tumour, and accordingly enhanced the ability to perform a safe radical tumour removal [35, 36, 41]. However, in some instances, post-operative sequelae, especially those involving the endocrine function, remain particularly challenging even in experienced hands, and should prompt some caution when speaking about "safe" radical resection [15, 34]. Likewise, neuropsychological disturbances are reported as a consequence of radical surgery [8], as well as an overall impairment of the quality of life. These considerations have prompted a measure of criticism about the effectiveness of the traditional surgical approach to CP, and suggested the possibility of alternative management options that exploit the possibilities offered by radiation therapy in all its aspects [2, 9, 19, 20, 30, 31, 37, 40]. The main criticism against radiation therapy is obviously the risk of degenerative changes in the surrounding highly functional areas, as well as the well-documented possibility of a late-onset vascular damage (mainly moya-moya disease) and the development of a second tumour within the irradiated volume [21]; and that is not a minor issue particularly when dealing with a pediatric population.

Our policy at the Catholic University, Rome, has always been to favor surgical excision of CP and to attempt radical tumour removal whenever possible. The controversies about the sequelae and the quality of life in patients—namely in children operated on for CP—prompted us to analyse the results of our treatment with the aim to verify weather an "aggressive" surgical management is really charged by such heavy post-operative sequelae so as to justify a more conservative approach.

## Patients and methods

Fifty-two children affected by CP were surgically treated at the Section of Pediatric Neurosurgery, the Catholic University Medical School, Rome, between January 1985 and December 2002. They represent approximately 8% of supratentorial tumours and 5% of all intracranial tumours operated on during the same period. Twenty-one children were admitted in the first decade and 31 in the second one. Thirty-three were males, and 19 females. Their age at diagnosis and treatment ranged from 20 months to 15.8 years (mean 9 years); in particular, 14 belonged to the 1–5 years age group, five being less than 2 years old; 25 were between 6 and 10 years old, and 13 more than 10 years old. However, when considering the onset of clinical manifestations, the first complaints were referred to an earlier stage, 11 months to 15 years (mean 8 years). Duration of clinical history ranged widely from 10 days to 12 years (mean 19.2 months, median 12.5 months).

The most prominent clinical manifestations were related to increased intracranial pressure (ICP) and to endocrinological and visual impairment (Table 1). Symptoms and signs of increased ICP were observed in 32 patients, and ranged from isolated headache to the complete picture of raised ICP syndrome. A dysfunction of the hypothalamic–pituitary axis was detected in 35 children with various combinations of the clinical manifestations. Twenty-three presented with growth retardation or low stature; 11 had clinical signs of reduced adrenocortical function (asthenia, systemic hypotension); ten had diabetes insipidus; five had retarded sexual maturation; and two had galactorrhea. An alteration of the alimentary habit was present in 12 patients, configurating a condition of hypo/anorexia with weight loss in nine instances, and a condition of hyperphagia with

**Table 1** Clinical findings of the 52 children at diagnosis

| Clinical signs and symptoms | No. of cases (%) |
|---|---|
| Increased intracranial pressure | 32 (61%) |
| Short stature | 23 (44%) |
| Reduction of visual acuity | 13 (25%) |
| Asthenia/arterial hypotension | 11 (21%) |
| Diabetes insipidus | 10 (19%) |
| Hemianopia/other visual field restrictions | 9 (17%) |
| Hyporexia and weight loss | 9 (17%) |
| Cranial nerve deficit (VI or III) | 6 (11%) |
| Retardation of sexual development | 5 (10%) |
| Hemiparesis | 4 (8%) |
| Gain ataxia | 4 (8%) |
| Seizures | 3 (6%) |
| Hyperphagia and obesity | 3 (6%) |
| Gynaecomasty/galactorrhoea | 2 (4%) |
| Nistagmus | 2 (4%) |
| Behavioral disturbances | 2 (4%) |
| Disregulation of the sleep–wakefulness rhythm | 1 (2%) |

obesity in three cases. Impairment in visual function was detected in 17 children, although only a few presented with this complaint; in particular, a deterioration of visual acuity was demonstrated in 13 children, and a visual field defect in 9. Neurological deficitary signs were observed more rarely. A 6th cranial nerve deficit was observed in five children, and a 3rd cranial nerve deficit in one case. Hemiparesis and ataxia were present each in four cases. Three children presented with epilepsy, two with behavioural changes, and one with alterations of the wake–sleep rhythm.

Pre-operative laboratory investigation revealed a complete deficit of pituitary function (panhypopituitarism) in ten cases, and selected hormone deficiencies in other 14 instances. The details of single hormone deficits are listed in Table 2. Mild to moderate increase in PRL levels was detected in six cases.

Neuroradiological work-up included CT scan and MRI in all but two cases (the first in our series who were investigated by means of CT alone). Cerebral angiography or, more recently, angio-MRI was utilised in selected cases to determine the precise relationship of the tumour with the surrounding vascular structures. On the basis of neuroradiological investigation the tumour appeared to be mainly cystic in 24 cases, solid–cystic in 20, mainly solid in eight. Calcifications of various degrees were present in 32 patients. As to tumour location, CP was intrasellar in three cases; sellar/suprasellar with prominent prechiasmatic growth in 24 cases, retrochiasmatic/3rd ventricular in 14 cases, and giant (with an extension into the middle and/or posterior cranial fossae) in 11 cases. As to tumour size, CP was judged to be small (<2 cm in diameter) in eight cases, medium size (2–4 cm) in 20, and large or huge (>4 cm) in 24. Obstructive hydrocephalus was present in 17 children and it was mainly associated with the retrochiasmatic variant (see also Table 3).

**Table 2** Pre-operative laboratory data of the 52 patients

| Hormone deficit | No. of cases (%) |
|---|---|
| Pan-hypopituitarism | 10 (19%) |
| Hypopituitarism | 14 (27%) |
| Deficit of single hormone | |
| GH, IGF-1 | 21 (40%) |
| ACTH, cortisol | 12 (23%) |
| TSH, FT3, FT4 | 7 (13%) |
| FSH, LH | 5 (10%) |
| Increased prolactin levels | 6 (11%) |

All the surviving patients were available for follow-up. Besides neurological, endocrinological and ophthalmologic examinations, all patients underwent seriated neuroradiological investigation. In particular, post-operative neuroradiological monitoring consisted of an early CT scan (within 48 h from the operation), and then by MRI (or less frequently CT) every 6 months for the first 2 years, and yearly thereafter.

## Results

### Surgical treatment

Surgical treatment consisted of a single operation in 47 instances and of a combined approach in the remaining five cases. In detail, 41 patients were managed by means of craniotomy alone (40 pterional and one subfrontal approach); six children were operated via the transsphenoidal (TS) route; four children underwent a TS approach followed by craniotomy, and one a craniotomy followed by TS approach. Trans-lamina terminalis approach was utilised in 14 cases, namely large retrochiasmatic or giant tumours. Radical tumour excision was the goal of surgical treatment in all the cases. The extent of tumour removal was assessed on the basis of post-operative contrast-enhanced CT scan, in adjunct to the impression of the operator. Total removal is defined as absence of any tumour remnant at post-operative CT scan, whereas "subtotal" usually indicates the presence of small amounts of residual tumour (less than 10% of the tumour left behind). In the case of CP, however, it is common experience to see on the post-operative CT scan some tiny flecks of calcium that remain stable at follow-up and that do not enhance after contrast administration (Fig. 1). Based on the data found in literature [35, 41], we also included these cases in the group of total resections. This result was achieved in 40 children (77%); subtotal resection was accomplished in nine cases (17%) and partial (more than 10% left behind) in the remaining three (6%). As expected, limited surgery was determined by intimate adherences between the tumour and

**Table 3** Pre-operative radiological findings of the entire series

| Tumor location and aspect | Number | Calcifications (%) | Contrast enhancement (%) | Hydrocephalus (%) |
|---|---|---|---|---|
| Intrasellar (all cystic) | 3 | – | 33 | – |
| Sellar/suprasellar prechiasmatic (71% cystic, 21% solid, 8% solid–cystic) | 24 | 58 | 37.5 | 17 |
| Sellar/suprasellar retrochiasmatic (77% solid–cystic, 23% cystic) | 14 | 84 | 38 | 46 |
| Giant (73% solid–cystic, 18% solid, 9% cystic) | 11 | 63 | 63% | 63 |

the surrounding structures (namely optic pathway, carotid artery, and hypothalamus) which prevented complete detachment of the capsule. If we match the extent of surgery with the anatomy, total resection was 100% in case of intrasellar tumours, 80% in those with a prechiasmatic growth, and 78% and 64% in case of large retrochiasmatic

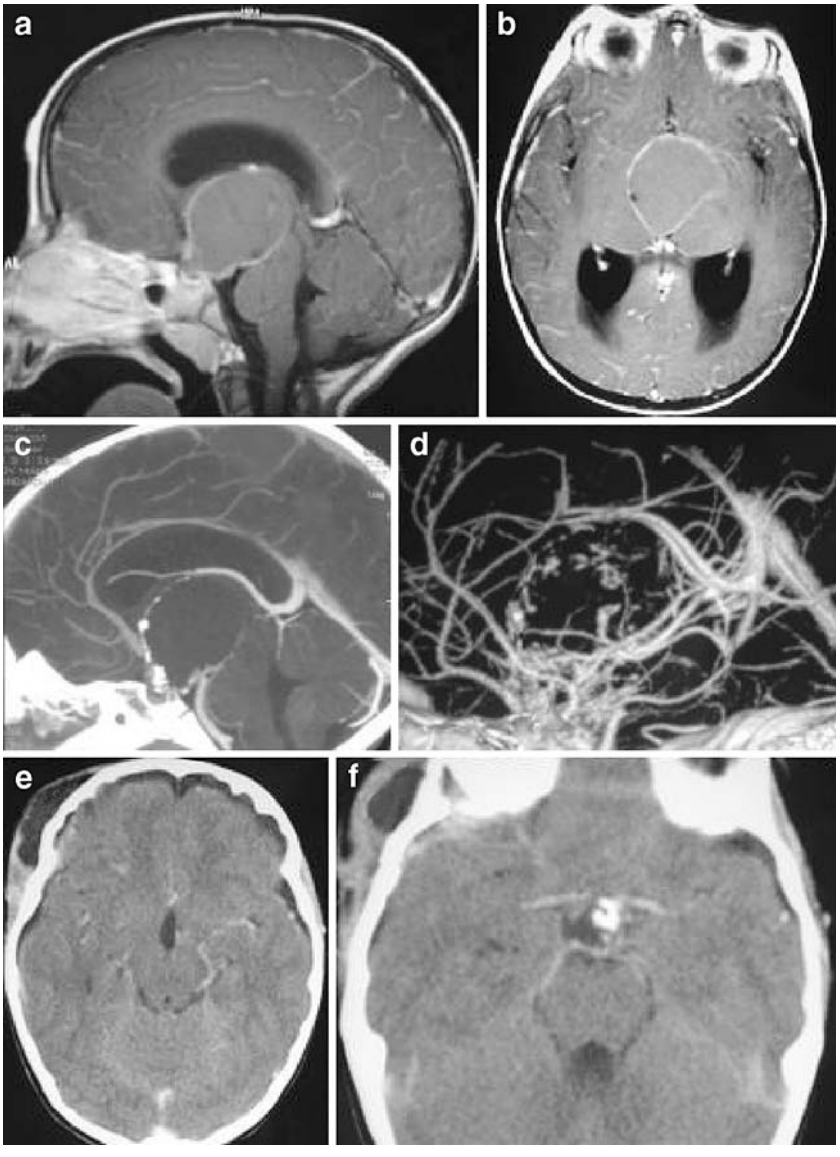


**Fig. 1** Pre- and post-operative neuroimaging of a 4-year-old girl. Pre-operative $T_1$-weighted sagittal (**a**) and axial (**b**) MRI, after gadolinium administration, shows the tumor extension within the third ventricle causing obstructive hydrocephalus. Note the ring enhancement of the tumoral capsule. Pre-operative CT sagittal reconstruction (**c**) and vascular 3D reconstruction (**d**) demonstrate the calcium deposits along the tumoral capsule and on the wall of the neighbouring vessels, indicating a subtotal removal of the lesion to preserve the integrity of the Willis' circle arteries. Immediate post-operative CT scan, after contrast medium administration, confirming the surgeon's intraoperative impression of the total removal of the tumor (**e**) with the exception of a calcium deposit, left in place intentionally, around the left internal carotid artery (**f**)

lesions and giant craniopharyngiomas, respectively. Moreover, it is obvious that the presence of huge calcifications was a prominent negative factor for radical resection.

The associated hydrocephalus that was present pre-operatively in 17 children required definitive surgical correction in seven of them. Two children underwent ventriculo-peritoneal shunting before craniotomy in consideration of the elevated risk of performing direct surgery in a condition of severely increased ICP. In seven cases, an external ventricular drainage was utilised to allow better tumour exposition, and it was removed within a few days in six instances. In the remaining child and in four further children, a permanent ventriculo-peritoneal shunt was implanted post-operatively for persistent derangement of CSF flow irrespective of tumour removal.

Details of the surgical treatment are reported in Table 4.

## Pathology

Histological examination revealed an adamantinous variant in all cases. The macroscopic aspect of the tumour was characterised by a cystic appearance with a cholesterol-rich, motor oil-like, thick brownish-yellow fluid content, sometimes with crumbly debris, in 44 cases. In detail, cystic–solid content was found in 33 cases and a pure cystic content in 11 cases. The remaining eight patients showed a mainly solid tumour. Macroscopic calcifications were present in 73% of the cases.

Microscopic examination revealed the presence of typical broad strands, cords and bridges of multistratified squamous epithelium with peripheral palisading of nuclei. Nodules of compact "wet" keratin and dystrophic calcifications were other common findings.

## Results of surgical treatment

(1) *Visual function* (Table 5). Out of 17 patients presenting with visual deterioration, seven showed an improvement of their pre-operative deficit, namely of visual acuity, and four remained stable; on the other hand, the remaining six children experienced a further visual deterioration. In particular, these novel deficits included a reduction in visual acuity in all of the six patients (until monocular amaurosis in two cases) and a visual field defect in three. The worse results were recorded amongst those with more severe pre-operative visual deficits and in those with mainly prechiasmatic CP.

(2) *Endocrine function* (Table 6). Post-operative deterioration of endocrine function was noted in 42 patients, configuring a hypopituitarism. In almost half of the cases, hormone deficiencies were already present prior to surgery, and operation further decompensated the pituitary function with the appearance of novel deficits. A new hypopituitarism was detected in 20 patients, and it occurred following craniotomy in 17 cases, a TS approach in one and a combined approach in the last two.

(3) *Transient diabetes insipidus* was almost the rule in the early post-operative period in case of craniotomy, whereas it was the exception in the case of TS approach. However, it subsided at variable time interval from the operation in almost 75% of the cases mainly following a craniotomic approach (only one case following TS surgery). On the other hand, three children experienced inappropriate anti-diuretic hormone secretion and hypoosmolarity. One of the last patients presented a prolonged comatose state.

(4) *Neurological function* (Table 5). Pre-operative hemiparesis and ataxia improved in all of the children presenting with this deficits, and then disappeared; likewise, with the 6th cranial nerve deficit. On the other hand, a new onset hemiparesis developed in four children, which was of mild degree in three cases and severe in one. Epilepsy developed in two cases, a transient 3rd cranial nerve deficit in two, and "peduncular" (Korsakoff-like) hallucinations in two. In one case, this particular complication was attributed to a basal ganglia myelinolysis sustained by the imbalanced water metabolism [12].

**Table 4** Surgical results

| Location (no.) | Approach (no.) | Total resection (%) | Shunts[a] | No. of recurrences[b] | Surgical resection of recurrences[c] |
|---|---|---|---|---|---|
| Intrasellar [3] | TS [3] | 100 | – | – | – |
| Prechiasmatic [24] | TS [2], C [18], C+TS [4] | 80 | 1 VPS | 4 (17%) | 2 total, 1 subtotal |
| Retrochiasmatic [14] | C [13], C+TS [1] | 78 | 2 VPS 1 SPS | 3 (21%) | 2 total, 1 subtotal |
| Giant [11] | TS [1], C [10] | 64 | 4 VPS 2 SPS | 2 (18%) | 1 total, 2 subtotal |

*TS* Transphenoidal, *C* craniotomy, *VPS* ventriculo-peritoneal shunt, *SPS* subduro-peritoneal shunt
[a]VPS was placed after tumour resection in all cases except three (one prechiasmatic, one retrochiasmatic and one giant)
[b]"True" recurrences occurred in one prechiasmatic (4%) and in two retrochiasmatic tumours (15%) (see text)
[c]The child with retrochiasmatic recurrence and multiple metastasis was treated by radiotherapy only

**Table 5** Comparison between pre- and post-operative other than endocrine deficits in the 48 survivors

| Pre-operative data | Number | Early post-operative data[a] | Number | Late results[b] |
|---|---|---|---|---|
| Intracranial hypertension | 30 | Improved | 27 | Resolved in all cases |
| | | Hygromas | 3 | Resolved by shunt |
| | | New cases: transient cerebral edema | 2 | Resolved by medical therapy |
| Visual deficits | 17 | Improved | 7 | Further improvement in all cases |
| | | Stable | 4 | Stable in 3, improved in 1 |
| | | Worsened | 6 | Stable in 4, improved in 2 |
| Neurological deficits[c] | 10 | Improved | 10 | Resolved in all cases |
| | | New cases: hemiparesis | 4 | Resolved in 2, stable in 2 (1 severe) |
| | | III c. n. deficit | 2 | Resolved in both cases |
| | | hallucinations | 2 | Resolved in both cases |
| Seizures | 2 | Stable | 2 | Resolved in 1, drug-responsive in 1 |
| | | New cases | 3 | Resolved in 2, drug-resistant in 1 |

[a]Within the first 3 months after surgery
[b]Median follow-up, 9 years
[c]Including cranial nerve deficits and hemiparesis

## Complications of surgical treatment

Two surgery-related deaths (3.8%) were recorded, both following a TS procedure. One fatality was the consequence of a massive intra-operative bleeding secondary to injury to the carotid artery, in an attempt to remove a calcification on the lateral wall of the sella. The second death was recorded on the fourth post-operative day as the consequence of a gram-negative CSF infection complicated by cerebral venous sinus thrombosis, following an otherwise uneventful TS tumour removal.

A transient discrete increase in subdural space was a relatively common finding, particularly in case of large or giant tumours. Only in three cases, however, did these subdural collections exert a mass effect and required surgical drainage.

## Late complications

One late death occurred 16 months after the completion of surgical treatment. This occurred in the above-mentioned subject, who experienced a prolonged comatose state. Although ultimately referable to the electrolytic imbalance, it was prompted by a major head trauma complicated by subacute subdural haematoma.

## Recurrences

Nine children, out of the 49 who survived the operation, presented a reappraisal of their CP at variable time interval from the completion of the surgical treatment. This corresponds to an overall recurrence rate of nearly 19%. True

**Table 6** Comparison between pre- and post-operative endocrine deficits in the 48 survivors

| Pre-operative data | Number | Early post-operative data[a] | Number | Late results[b] |
|---|---|---|---|---|
| Hypopituitarism | 22 | Improved | 5 | Hormonal therapy in 4 |
| | | Stable | 11 | Hormonal therapy in 8 |
| | | Worsened | 6 | Hormonal therapy in 5 |
| | | New cases | 20 | Hormonal therapy in 14 |
| Short stature | 21[c] | Stable in all cases | 21 | Normal stature in 13 |
| | | | | Hypostaturalism in 8 |
| Weight alterations | 10 | Improved | 4 | Normal weight in all cases |
| | | Stable | 5 | Normal weight in 2, obesity in 3 |
| | | Worsened | 1 | Obesity |
| | | | | Late obesity in other 5 cases |
| Diabetes insipidus | 9 | Improved | 1 | No therapy |
| | | Stable | 7 | ADH in 2, resolved in 5 |
| | | Worsened | 1 | ADH |
| | | New cases | 29 | ADH in 17, resolved in 12 |

*ADH* Anti-diuretic hormone
[a]Within the first 3 months after surgery
[b]Median follow-up, 9 years
[c]Five children underwent hormonal treatment before admission

recurrences, i.e. novel appearance of tumour after an apparently gross total removal, should be kept separate from re-growth of residual tumour left behind at operation. In this light, only three children presented "true" recurrences—4, 4.6, and 6 years after the operation. It is worth noting that in two cases tumour relapse occurred relatively away from the original site. In one case, the recurrence was inside the 3rd ventricle, whereas in the other child a relapse occurred initially along the previous surgical route, and then, after its removal, multiple supra and infratentorial localisations were detected which required radiation therapy [27]. In contrast, the remaining six children presented a re-growth of their residual tumour. Most of these relapses were asymptomatic, and only one child presented with progressive visual loss and signs of increased ICP. In the light of the previous distinction, the recurrence rate in case of total resection is actually of 7.7%, whereas it reaches 50% in case of less than total resection.

All the recurrences were treated surgically. Previous surgical access was utilised in all the cases with the exception of the 3rd ventricle relapse, which was managed via an interhemispheric transcallosal approach. As expected, the arachnoidal adhesions made difficult, or even precluded in some cases, the development of a safe cleavage with brain cortex. Nevertheless, a gross total resection was achieved in five cases and a subtotal/partial in the other four. One post-operative death was recorded, corresponding to a surgical mortality for recurrences of 10%. This was the case of the child who underwent the operation in an already compromised general condition secondary to severe hypothalamic damage.

### Radiation therapy

Radiation therapy (RT) was administered post-operatively to 12 children. Six patients underwent RT after an initial incomplete tumour removal: five children were treated by means of standard RT (54 Gys) and one with γ-knife. Only one of these six patients experienced tumour relapse. In adjunct, RT was administered to six of the nine patients with tumour recurrence (five standard and one γ-knife).

One boy, who received RT following re-operation for a delayed relapse 6 years after an initially gross total tumour removal, experienced the novel development of a malignant thalamic glioma 8 years after the completion of RT. This second tumour was partially resected and is presently being treated with chemotherapy.

### Late follow-up

Out of the original 52 patients, 48 were eligible for follow-up. All of them are alive from 2 to 20.5 years from the operation (median 9 years, mean; 8.5 years). The most relevant aspects of their clinical status are listed below (see also Tables 5, 6).

(1) *Visual function.* A mild improvement in visual acuity was demonstrated in up to 50% of the cases at late follow-up, whereas visual field defects remained stable. Reduced visual acuity or visual field defects, however, were not so invalidating as to prevent all the affected patients from participating in a normal social and school activity. Only one girl, who was already amaurotic at admission and did not improve after tumour removal, has requested special schooling.

(2) *Endocrine function.* Thirty-one patients present hypopituitarism and rely on hormone supplementation. Twenty-eight patients are on hydrocortisone medication for adrenal insufficiency, and 24 on thyroid hormone replacement. Twenty-one children with low stature have received or are receiving growth hormone (GH), with an increment in their height and/or normal stature in 13 cases (62%). In 38% of the cases, however, the definitive stature remains below the 2 SD, irrespective of hormone replacement. In our experience, GH therapy did not influence tumour recurrence (only one girl relapsed in concomitance with the starting of GH therapy). At the time of pubertal maturation, specific sexual hormone replacement was started in eight patients. In spite of the apparently good endocrinological control, nine patients (19%) (those with initial severe hypothalamic involvement) presented frank obesity, whose management is a major problem. It is worth noting that the lamina terminalis was opened in five of these nine children. Early post-operative diabetes insipidus subsided at variable time interval from the operation in almost 78% of the surviving patients. A definitive ADH deficiency was evident in 20 children (43%).

(3) *Neurological function.* Only two patients presented a stabilised hemiparesis, which is severe in one case. Two patients are on anti-epileptic regimen for epilepsy and one of them showed relatively drug-resistant seizures.

(4) *Psychological and social function.* With the exception of two girls (one amaurotic and the other with residual hemiparesis and epilepsy), all the other patients enjoy a normal social life. Although present in nine cases, obesity does not represent a major social limitation for any of them. Most children have attended (or are attending) normal schools.

## Discussion

In spite of the continuing progress in microsurgical techniques and of the sophisticated operative aids currently available to the neurosurgeon, the treatment of CP still constitutes a major problem, particularly in children [7, 14,

22, 36]. The peculiar anatomy of the suprasellar region and the relationship of the tumour with the surrounding vital and functionally relevant structures are the reason for the difficulties faced when performing tumour removal. Without considering the risk of life, visual, endocrine and neurological functions can be severely compromised in the attempt to dissect free the tumour from the optic pathway and hypothalamus, as well as from the carotid artery and its main branches.

The risks inherent to the surgical treatment of CP are even more relevant in children. Actually, most of these tumours manifesting early in life have some distinguishing features from their adult counterpart that make their management even more problematic. In fact, childhood CP is often of large or huge size compared to small- or medium-sized tumours found in adulthood [3, 5, 7]. The adamantinous variant is prevalent, whilst the papillary or mixed type are almost absent [1, 39]. The recurrence rate, which is a function not only of the extent of surgical removal but also of the histology, is higher in children compared to adults even following an apparently gross total removal [1, 6, 23, 29]. The retrochiasmatic variant, which is associated with more relevant hypothalamic involvement, represents almost 50% of the cases, whilst the intrasellar one is quite rare [5, 38]; as a consequence, obstructive hydrocephalus complicates the clinical picture in about one third of the cases. The reason for this behaviour is not obvious, although one might speculate that the early clinical appearance of an assumedly congenital tumour would suggest an increased biological aggressiveness.

All these considerations justify the increased concern in dealing with this tumour in children. The reduced rate of total resections obtained in children compared to adults (not only in pediatric series but also in those reporting on a mixed population) seems to underline these increased difficulties [4, 22, 32, 36]. Apart from the surgical challenge, the post-operative management can be particularly complex, especially for the aspects of the water and electrolytic balance that can hamper the patient's life at any moment. Furthermore, aside from the well-recognised hormonal deficiencies and visual deficits related to tumour location, patients are now acknowledged to experience pathologic obesity and deficits of higher cortical functions, memory, and behaviour [8, 11, 33]. The combination of these deficits can have profoundly detrimental effects on their quality of life [18]. Patients with CP rated their health-related quality of life as considerably lower than healthy controls; the domains of social and emotional functioning were particularly affected [28].

Severe obesity represents another major concern after CP removal. It is usually associated with higher tumour volume, a higher rate of a hydrocephalus requiring a shunt, and of hypothalamic involvement [26, 34]. The body mass index at the time of diagnosis is significantly higher in patients who develop post-operative obesity than in those who do not. Unfortunately, post-operative GH therapy that can induce excellent linear growth often fails to have an ameliorative effect on weight gain [13].

The main goal in the treatment of a benign tumour should be its radical removal with absent or minimal functional impairment. Unfortunately, this goal is only partially achieved in the case of CP. For many years neurosurgeons have dedicated every effort to accomplish a safe radical removal. Accordingly, the percentages of radical resection have progressively increased from the pre-microsurgery era, reaching even 90% of the cases [15, 41]. Increased surgical ability and a more sophisticated post-operative endocrinological management have significantly lowered surgical mortality and morbidity.

Most surgical series express the results of treatment of CP in terms of percentage of total resections and rate of recurrences. However, this point of view is quite limited in the case of children who have a lifelong expectancy. The need for continuous hormone replacement may represent a limiting factor for an acceptable quality of life; likewise, the above-mentioned risk of obesity. In certain subgroups of patients, such as those with large tumours and hypothalamic extension, primary surgery is associated with a high incidence of complications and high failure rates. Poor functional outcome is often associated with large tumours infiltrating or displacing the hypothalamus; likewise the occurrence of hydrocephalus (diagnosed at a young age) and multiple operations due to tumour recurrence, are all detrimental factors for long-term outcome. These considerations have prompted some neurosurgeons to adopt an individualised risk-based treatment approach that attempts at maximising cure rates without compromising long-term functional outcome. Operatively, this translates into a less aggressive approach to pediatric CP, favoring sub-total tumour resection followed by radiotherapy as an alternative to total removal [10, 14, 17, 32].

Our policy was always to attempt at a radical tumour resection; this was achieved in 77% of the cases, which seems in agreement with the standard results reported in the literature [25, 35]. At any rate, a "radical" surgical attitude, which means the attempt to remove as much tumour as possible, was adopted in up to 94% of the cases (corresponding to the sum of the purely gross total resections and of the subtotal ones). Only in a very limited number of patients was the surgical attitude towards a limited resection adopted. These results were obtained by means of a unique approach in 90% of the cases, and a combined approach was utilised in the remaining 10%. We favoured the pterional approach in almost all cases undergoing craniotomy; only in two cases we choose a different approach: the bilateral frontal and the transcallosal route. According to previous reports in the literature [16, 24, 25, 41], and also based in our experience, the pterional approach gives a superb view of the tumour and can allow safe detachment of the capsule from the surrounding structures. We do not believe that the more ex-

tensive frontal approach represents a real advantage in managing this type of tumour. On the other hand, opening of the sylvian fissure often proved to be more complex than in cases of other tumours with similar location, because of the presence of tenacious adherences or even of a hypoplasic fissure. Although this phenomenon might represent just an anatomical variant, one may speculate of a chemical arachnoiditis due to spillage of the cyst content into the subarachnoid space to be responsible for these increased difficulties in developing a safe arachnoidal plane around the tumour. In several cases characterised by severe ventricular dilatation, we found advantage in the use of and external ventricular drainage positioned just before opening the dura; this manouvre, in fact, allowed the reduction of extensive brain traction.

Post-operative subdural hygroma is a known complication of many craniotomic approaches, favoured by opening of the subdural space. This complication was not rare, although it required surgical correction only in a few cases, all characterised by severe pre-operative hydrocephalus. The utilisation of a peri-operative external drainage may help to obviate this complication by allowing surgeons to refill the empty ventricular system at the end of the operation, thus inducing parallel re-expansion of the cerebral cortex.

The recurrence rate in our series parallels those reported in series with sufficiently long follow-up [17, 25, 36]. In fact, since the recurrence rate is a function of the duration of follow-up (the longer the follow-up the higher the number of recurrences), the reduced recurrence rates reported in some series probably corresponds to a limited post-operative observation. Apart from the re-growth of tumour remnants in the case of incomplete resection, true recurrences were quite rare. These occurred relatively distant from the previous tumour, and in one case the relapse occurred along the surgical corridor utilised for the previous approach and, after its resection, again in more distal locations [27].

RT was utilised after an initially incomplete resection only in selected cases, and always in children more than 4 years old. We are reluctant in utilising RT in cases of subtotal removal, as many of these residual tumours can remain stable at follow-up even without any adjuvant therapy. Accordingly, we initially followed up our patients by means of neuroradiological monitoring, and we do not suggest any adjuvant treatment if residual tumour remains stable for 3 years, as relapse of these remnants usually develops within the first 3 years after operation. Accordingly, we suggested RT only in cases of large residuals or in cases of small remnants manifesting a re-growth. On the other hand, RT represents, in our opinion, a reliable instrument in case of relapse as an adjunct to surgical therapy.

On this regard, the experience of a malignant glioma developing 8 years after standard RT for a recurrence seems to raise some caution on a too liberal utilisation of this therapy. A very limited number of malignant gliomas developing after radiation therapy for CP have been reported in the literature [21]. In most cases, the secondary tumour is seen at the edge of the irradiated volume, and not in the region with the highest absorbed dose. Although rare, this represents a dramatic late event charged of a heavy prognosis. The mean latency period between irradiation and evidence of the "second" tumour is 10.7 years (median 9.6 years). It is worth noting that the shortest latency periods have been reported in patients who had received GH therapy. Although a life-long follow-up is mandatory to seriously answer the questions about therapy-induced secondary neoplasms for all patients who are survivors of childhood cancer, the need for GH replacement in children operated on for CP should suggest a cautious attitude in suggesting RT, even in the case of incomplete resection.

Overall, adopting the traditional neurosurgical parameters for assessing the efficacy of surgical treatment, the results of our treatment of CP should be regarded as "good". In fact, most of the children in our study are alive and in good condition. Visual defects, including one amaurosis (the girl who was already amaurotic at admission), represent a major concern only for a very limited number of patients. The endocrine function, although compromised in about three fifths of the cases, is managed with ease by means of single or dual hormone supplementation. Definitive diabetes insipidus is present in about two fifths of survivors. Short stature has been corrected in two thirds of the children presenting with this pre-operative complaint, and ameliorated in one third. Pathologic obesity afflicts nine patients with initial severe hypothalamic involvement. However, social life is heavily affected only in two cases. These results would suggest the consideration of our approach to pediatric CP as a correct one.

Although aware of the potential benefits of a more conservative approach, at the same time we are worried about the potential detrimental effects of RT, not only for the rare possibility of a "second" tumour, but also for the well-documented possibility of vascular derangement (namely moya moya disease). Accordingly, we believe that the initial treatment of CP should be its total resection whenever feasible according to the anatomy of the tumour. On the other hand, a less aggressive attitude might be a good alternative in case of huge tumours invading the hypothalamus, for which attempts at radical surgery are usually weighted by more severe post-operative complications.

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