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Treatment of Craniopharyngiomas— the Stereotactic Approach in a Ten to Twenty-Three Years' Perspective

I. Surgical, Radiological and Ophthalmological Aspects

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Summary

A multi-modality treatment programme, where stereotactic methods were used preferentially, gave results in a consecutive series of craniopharyngiomas, not inferior to those reported after microsurgical removal. Fourty-two patients with a follow-up range of 10–23 years are reported.

Keywords: Craniopharyngioma; stereotaxy; intracavitary irradiation; radiosurgery.

Introduction

In spite of all the technical advances in the modern management of intracranial tumours, the treatment of craniopharyngiomas still offers difficulties. Few controversial topics attract so much attention at neurosurgical meetings as does the therapy of these tumours. Many pictorial descriptions of this special surgical challenge are found in the literature; the tumour "leads the neurosurgeon bravely on only to defeat his dissection, outmanœuvre his microscope and defy his ambitions"[28].

Thus, many papers on this topic mirror their authors' ambivalence and indetermination. This still holds true now in the eighties, but was seen even more often 25 years ago, when the present study was initiated.

The utilization of stereotactic methods for so-called non-functional operations implied new options in brain tumour surgery[3]. The principal features of a stereotactic treatment protocol for craniopharyngiomas were outlined long ago[19]. Based upon this, a treatment programme was initiated at the Karolinska Institute during the early sixties, and has been followed consistently since 1964[1, 2, 4–6, 19].

The biological character of craniopharyngiomas implies that definite results of any treatment can not be estimated with certainty until after a very long follow-up period[9]. Recurrent tumour may occur in a patient, who has been considered tumour-free at a previous follow-up. It is crucial, that the evaluation of a radically new and different therapeutic approach is made with particular respect to this. As our experience has been gained over more than 25 years, it now seems appropriate to evaluate the stereotactic policy.

Ionizing radiation was used as a main tool in the present study. Usually, the only treatment was intracavitary irradiation of tumour cysts, using injected liquid radiocolloid. Some patients had external irradiation exclusively, or as an adjunct to other treatment modalities. The following semantic distinction is used in this paper:

Radiosurgery: Stereotactically directed, multi-portal single dose irradiation (with the "Gamma Unit"[18]).
Radiotherapy: Fractionated radiation treatment of a more conventional design (linear accelerator).

Material and Methods

During 1964 and 1976, 42 consecutive patients with a previously untreated craniopharyngioma were admitted to the Department of Neurosurgery, Karolinska Hospital. The selection criteria for the present study are listed in Table 1. There were 24 males and 18 females, from 5 to 63 years of age (mean 25.3). The age distribution is shown in Fig. 1.

The diagnosis was primarily based upon radiological and clinical features, and the criteria used are discussed in a previous paper[4], including the first 16 patients of the present material.

Table 1. *Selection Criteria and Case Material*

1. Radiological/clinical diagnosis of craniopharyngioma
2. Consecutive patients from 1964-1976
3. No previous treatment
4. Thorough follow-up in 1987 (observation period 10 years or more)

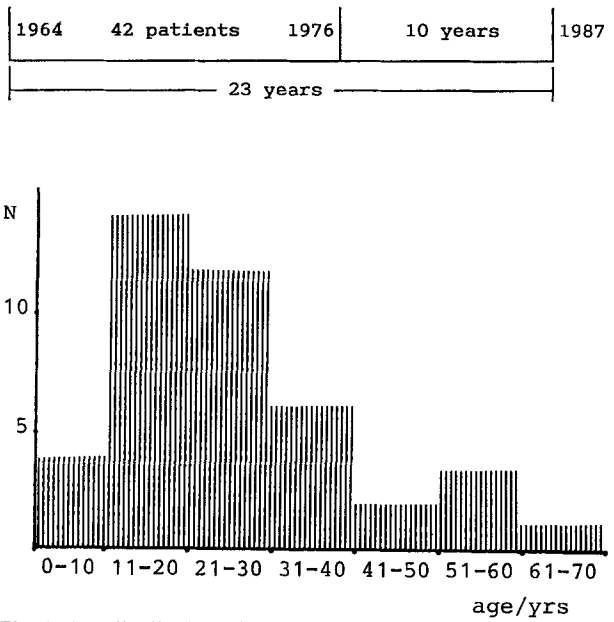

Fig. 1. Age distribution of the whole material

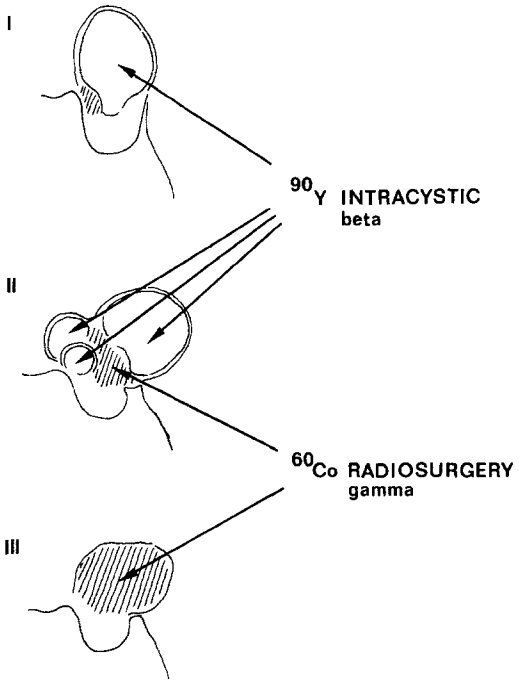

Fig. 2. Management policy for the stereotactic treatment (see text)

The patients were categorized into three groups[7], those having predominantly cystic lesions, with an insignificant solid part (Type I, N=24), those with polycystic tumours, with appreciable solid portion, (Type II, N=11) and those with usually small, predominantly solid tumours (Type III, N=7). The individual treatment programme was based upon this morphological classification (Fig. 2) and the assumption, that clinical problems in craniopharyngiomas most often are due to expanding cysts, whereas solid tumour parts often remain relatively quiescent. The stereotactic methods used have been described in detail previously[7].

The surgical management in each patient included an exploratory stereotactic puncture as the first step. As a rule, Type I and Type II tumours could then be given intracavitary treatment with yttrium -90 in a colloidal solution (YAS-3-P, Amersham, England). Patients with polycystic tumours had the two (or three) largest cysts treated at the first procedure or were re-admitted for consecutive treatment of one cyst after the other, with a period of months in between. For the entirely solid tumours (Type III), radiosurgery was used as the first choice, in some cases after a stereotactic biopsy. All stereotactic operations were routinely performed under local anaestheasia only; general anaesthesia was however used in the paediatric patients.

25 patients were thus treated with stereotactic methods exclusively, intracavitary irradiation of cyst(s) and/or radiosurgery. In another five, initially treated by stereotactic methods, further treatment was considered necessary and they were additionally treated with open, surgical removal (four cases) and radiotherapy (one case), respectively. The eventual treatment in the remaining 12 was surgical removal (nine), radiotherapy (one) and a combination of these two modalities in two patients (Table 2).

Of those patients who were treated with surgical removal and/or radiotherapy, five tumours were very large (all Type II), they had a larger number os small cysts and an appreciable solid part.

Six patients had open surgery as the only treatment albeit their tumours were monocystic (Type I) and would thus have been suitable cases for yttrium treatment. In these cases the initial explorative stereotactic puncture disclosed the cyst contents to be rich in cholesterol which made the aspiration difficult. As the effect of any intracavitary treatment thus would have been difficult to predict, yttrium was omitted and the tumour was removed, using open surgery.

Follow-up

The review was initiated early during 1987 and was completed within the same year. The range of the observation time was then 10–23 years (Table 1). It was possible to trace all patients but one, a patient living abroad. Ten patients were dead, thus 31 patients remained for evaluation. The various treatments and the over-all outcome is comprehensively shown in Table 2. The survivors were seen on an out-patient basis early in 1987, with a complete laboratory work-up included. In most cases, a follow-up CT was performed at the Karolinska Hospital, but in the remainder, one of the authors (C.-G. Bergstrand) organized adequate radiological check-up at the patient's local hospital, but the X-ray material was assessed by him personally.

The ophthalmological follow-up had a similar design; the patients were seen by the ophthalmologist of the group (L. Tallstedt), who also evaluated results from all the previous examinations.

The patients' endocrine and general functional state was evaluated by the endocrinologists (M. Sääf, M. Thorén).

The results are presented in a twin paper (Sääf *et al.* in this issue),

Table 2. *Treatment Modalities and Total Outcome.* A. Intracystic isotope (Yttrium-90). B. Stereotactic external single dose irradiation. C. Surgical removal. D. Conventional radiotherapy (linear accelerator).

Modality	N	Alive and well	Death due to tumour	Death, intercurrent disease
A	17	14	–	3
B	4	3	–	1
A and B	4	4	–	–
A and C	4	2	2	–
A and D	1	–	1	–
C	9	8	1	–
D	1	lost for follow-up		
C and D	2	–	2	–
	42	31	6*	4**

*All tumours large/huge, polycystic (Type II), failure rate in 10–23 years perspective: $^{6}/_{42}$ = 14.3%.
**Autopsy: No recurrent tumour (3), "suprasellar cyst" (1).

but are described shortly here. Of the 31 patients evaluated at the endocrinological follow-up, two had normal anterior pituitary function, eight had partial insufficiency and 21 panhypopituitarism. Diabetes insipidus was found in four patients with partial pituitary insufficiency and in seven with panhypopituitarism.

The pituitary function in the ten dead patients was interpreted in retrospect, from data in the patient's chart, achieved at the last examination before death. Eight then had panhypopituitarism (in five with concomitant insufficient ADH secretion), one a partial insufficiency and only one out of the ten had normal pituitary function.

Results

The outcome in the whole series is comprehensively shown in Table 2.

As the main aim of this study was to critically evaluate the stereotactic methods, the results in the 25 patients treated with such technique exclusively are summarized here. The results were particularly mirrored in the CT findings and in the ophthalmological results.

The radiological findings at the follow-up are summarized in Table 3.

Table 3. *Follow-up CT in Patients Treated by Stereotactic Methods Exclusively (N=21)*

Tumour type	No expanding lesion/ no contrast enhancement/ insignificant tumour remnants	Marked reduction of initial tumour size
I	13	1
II	4	–
III	3	–
	20	1

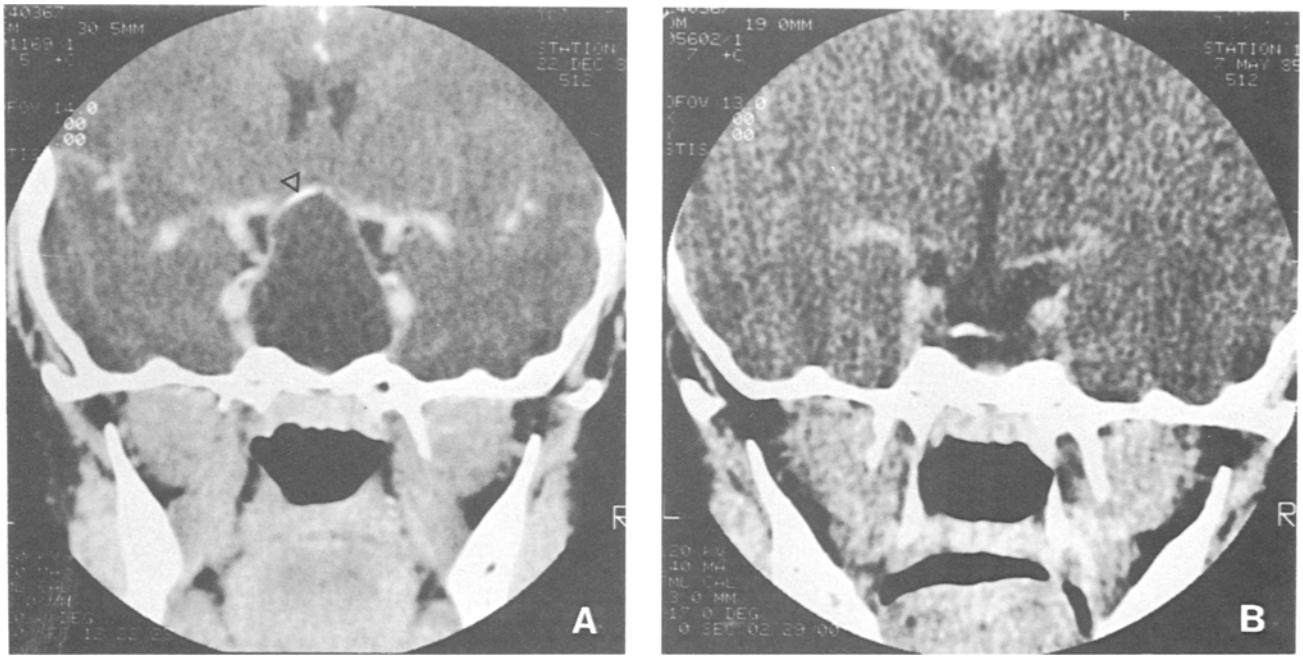

Fig. 3. A recent case of a Type I tumour illustrates the effects after the intracystic yttrium irradiation. A) Preoperatively a large intra- and suprasellar cyst is seen, the capsule partly calcified (arrow). B) Eighteen months after treatment, the cyst is shrunken into the sella, leaving the suprasellar cisterns open and free from adhesions to the surroundings. The capsular calcification can now be seen entirely intrasellarly

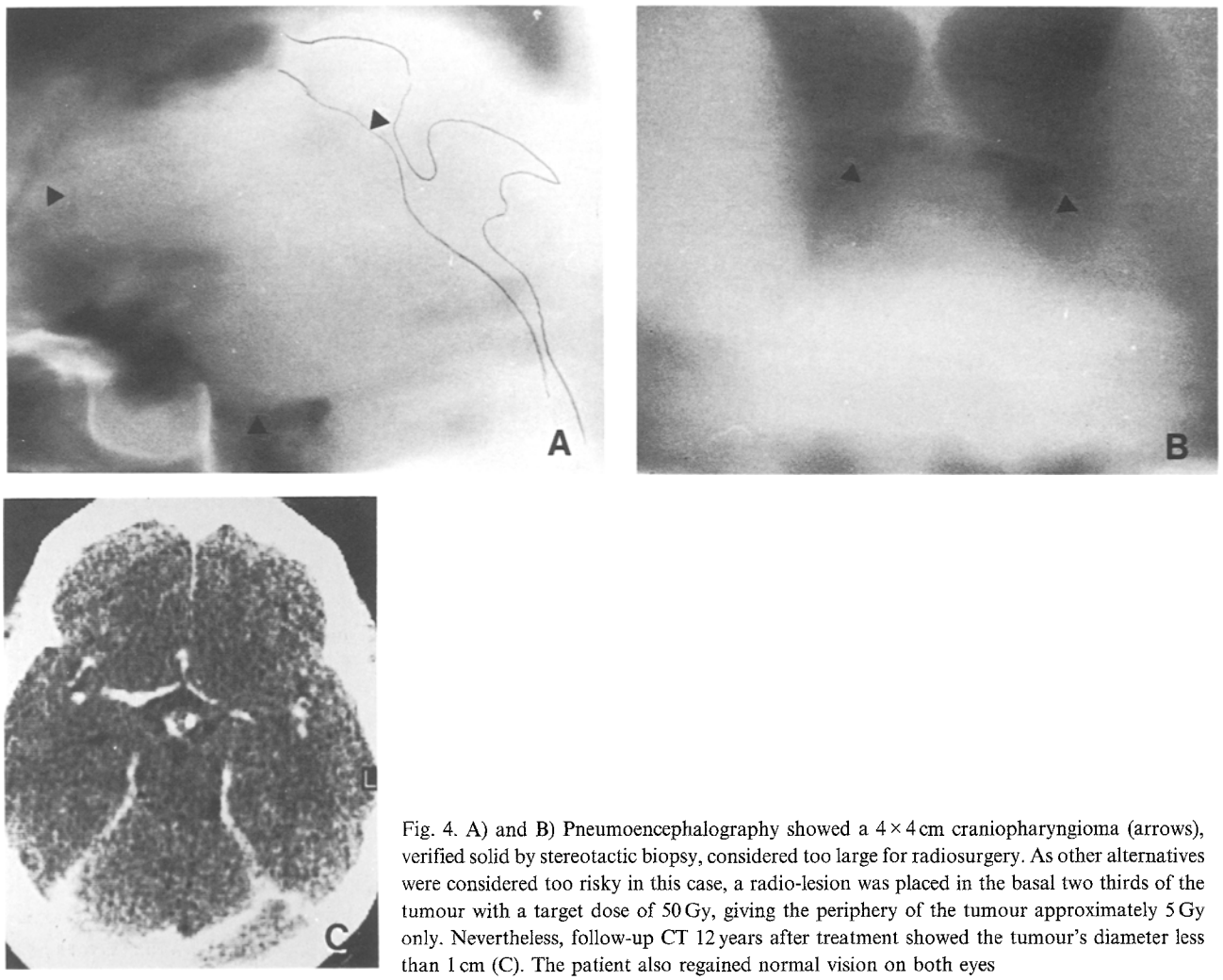

Fig. 4. A) and B) Pneumoencephalography showed a 4 × 4 cm craniopharyngioma (arrows), verified solid by stereotactic biopsy, considered too large for radiosurgery. As other alternatives were considered too risky in this case, a radio-lesion was placed in the basal two thirds of the tumour with a target dose of 50 Gy, giving the periphery of the tumour approximately 5 Gy only. Nevertheless, follow-up CT 12 years after treatment showed the tumour's diameter less than 1 cm (C). The patient also regained normal vision on both eyes

The yttrium injection as a rule caused a pronounced and permanent shrinkage of the tumour, in many cases a virtual radiological disappearance, combined with an opening of the cisterns around the tumour, sometimes as pronounced as a herniation of the suprasellar cisterns into the sella turcica (Fig. 3). These changes were gradual, and as a rule, the shrinkage was not complete until after many months. Occasionally, the decrease of the cyst size after the yttrium injection was slower than expected. A re-puncture, with a mere aspiration of the contents, most often initiated the definite and complete cyst collapse. In seven cysts, a second yttrium injection had to be given, to achieve this. Solid tumour parts, treated by radiosurgery, also diminished gradually in size, but usually not as markedly as did the cystic parts after the intracavitary yttrium treatment[6]. Occasionally, however, spectacular results were seen (Fig. 4).

In this group of patients treated by stereotactic methods only, 20 had complete pre- and postoperative ophthalmological records. (One patient of the 21 alive for follow-up had no preoperative examination.) The results regarding visual acuity are diagrammatically shown in Fig. 5.

Visual field defects were found in 29 eyes preoperatively and in five of these, more than two quadrants were affected. Two patients had homonymous defects but bitemporal defects were the most common pattern. At follow-up, 27 eyes had defects, but of the 29 eyes, with defects preoperatively, four had normal fields, another four were unchanged, 13 were improved and eight were worse. Thus two eyes (in the same patient) with normal fields preoperatively had defects at the follow-up.

Ten eyes had atrophic optic discs preoperatively. In one patient an abducens nerve paresis was seen before

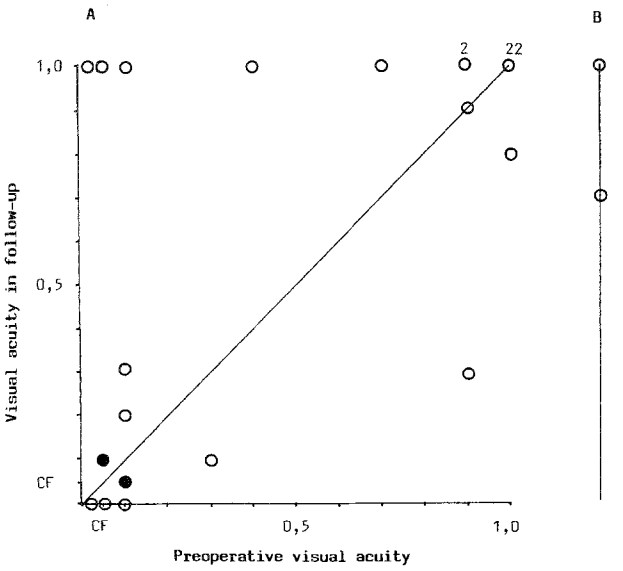

Fig. 5. Visual acuity of 21 patients (42 eyes) treated by stereotactic techniques exclusively. A) Preoperative values (abscissa) plotted against the follow-up values (ordinate) in the 20 patients with both preoperative and follow-up examinations. Each circle represents one eye (figures in the upper right represent 2 and 22 eyes, respectively). The two black dots represent amblyopic eyes. (*CF*=counting fingers). B) Follow-up values in the one patient without preoperative examination

treatment but no eye muscle weakness was seen in any patient at follow-up.

Adverse Effects

In the total material of 42 patients, there were no peroperative complications. In one case, a slight hemiparesis contralateral to an explorative puncture was seen during the immediate postoperative period. Angiography revealed spasm of the A 1 segment of the circle of Willis on the punctured side. A mechanical impact from the puncture cannula might have been responsible for this, but irritation from cholesterol-rich cyst fluid leakage into the basal cisterns might also have been the cause. The neurological symptoms disappeared gradually with full recovery. Another patient experienced a fairly sudden diplopia nine days after an yttrium installation, due to a 3rd nerve paresis. A noxious effect from the yttrium was suspected and the cyst contents was aspirated. This made the oculomotor palsy worse. The cause remains obscure, but some kind of mechanical influence (stretching of the cyst capsule, e.g.) might have been the noxious factor.

In one case, a late adverse effect from the radiation was suspected. This patient had seriously impaired vision on her first admission, 1.0 right and finger counting left, due to a monocystic tumour. After yttrium treatment, the patient regained vision completely in her left eye. However, nine months later, she was readmitted because of rapid deterioration of the vision of her left eye. A microsurgical exploration was then performed. No tumour was found and the optic pathways were without gross changes except a small translucent area in the left optic nerve. The eye remained blind and the irradiation might have been the noxious factor for the optic nerve, however previously severely damaged by the tumour.

Fatalities

The overall mortality is presented in Table 2. Out of those patients treated with stereotactic methods exclusively, four patients were dead, all from intercurrent disease/condition, without evidence of tumour recurrence. In one, a five-year-old boy, a satifactory collapse of a Type I tumour was proven by pneumoencephalography. Three and a half years after this, the patient was brought in as an emergency to a local hospital with high fever and jaundice. In spite of intense therapy, he succumbed from an acute infectious hepatitis and aplastic anaemia. This boy had panhypopituitarism. Autopsy showed insignificant tumour remnants above the diaphragma sellae, completely without adhesions to the surrounding normal structures.

In two more patients, who died from acute obstruction of a ventriculo-venous shunt and leukemia, respectively, autopsy showed tiny, completely insignificant intrasellar tumour remnants.

The fourth dead patient of this group was an elderly man, who died suddenly at home, ten years after the treatment. He was the patient with the treatment-induced diplopia, described above. Less than one year before his death, an X-ray check-up showed his tumour to be 19 × 11 × 6 mm, a significant decrease from its original size. Clinically, he had no sings of recurrent tumour and his oculomotor paresis was now almost absent. Autopsy at a local hospital revealed subarachnoid haemorrhage, the source being an "erosion of the posterior communicating artery". The occurrence of a "suprasellar cyst" is further shortly mentioned in the autopsy report.

In the total material, six more patients had died. In these, it had been very difficult, despite various therapeutic measures, to cope with large, aggressive tumours, all of Type II. Four of them must be considered therapeutic failures. One of these did very well initially after cyst treatment only and lived in a good condition

for nine years after treatment. After a fairly sudden recurrence, he was sent to a renowned surgeon in another country for an attempt at radical removal. The patient died soon after this operation. The tumour was found to have an irregular, para- and retrosellar growth and was obviously inoperable. Even the original monocystic tumour, treated with yttrium initially, had an unusual location, growing almost entirely in the middle fossa.

Two patients are considered as failures, albeit the immediate cause of death was probably not directly related to the tumour. One, a small girl, died suddenly at her home during an acute infectious disease. Acute adrenal insufficiency was discussed as a causative factor. She had a remaining tumour of significant size, although markedly smaller in size than at the time of treatment.

A similar case was that of a young man with seizures, who died in connection with his epilepsy. After successful yttrium treatment of three cysts, his tumour seemed to be of stable size. Nevertheless the remaining tumour bulk means that this case also has to be considered a failure.

Discussion

The stereotactic treatment policy differs markedly from the widely used and commonly accepted one of radical tumour removal. When stereotactic treatment is used exclusively, the admission period seldom exceeds a couple of days, in striking contrast to the extended hospital stay often necessary after extensive surgery. In the present material, there were neither operative deaths nor peroperative complications, but some suspicions of side effects from the treatment were entertained later. An analysis of these indicate that they may be avoided by improved technique. A cautious study of the individual vascular anatomy, e.g., is of course mandatory for a safe selection of the needle trajectory at the stereotactic puncture. Proper attention was apparently not paid to this in one case, where transient arterial spasm probably was induced by the puncture cannula.

The possible risks for an adverse effect from the intracystic irradiation could be avoided in the next series by minor changes of the technique. Colloidal phosporous-32, which was used by our group in some tentative cases before the present study[19], is now available in new and better preparations and would probably be superior to yttrium-90, as the beta radiation from P-32 has a shorter range. An alternative to radioactive material for the intracavitary treatment should also be discussed. Interesting results have been obtained with the use of intracavitary bleomycin[34].

It has been argued that radiation may induce adhesions and scarring in the vicinity of intracranial tumours treated with intracystic irradiation, thus making later attempts at microsurgical dissection difficult and even hazardous. A striking feature of the follow-up radiology in the present material is the persistence of open cisterns and even spatious conditions around the tumours thus treated (Fig. 3). This has been verified in patients operated on after yttrium treatment (Penzholz, pers. comm.). Thus, contrary to what is claimed, stereotactic treatment as the first choice might even *facilitate* later open surgery, should it become necessary.

When reading reports on craniopharyngioma surgery, it is often difficult to evaluate the true meaning of terms like "radical removal", "total excision" etc. It is a well-known fact to the experienced surgeon, that a craniopharyngioma often baffles the surgeon's aims to remove it radically. Thus, the reader's attention is directed particularly to the outcome in patients reported to have had their tumour completely *removed* and less to those, where the degree of operative radicality is described in unprecise terms.

A tentative interpretation of diverging figures on surgical radicality, from the most recent literature, indicates the real possibility of *total virtual removal* of a craniopharyngioma, even in experienced hands and using modern microsurgical technique, to be surprisingly low (Table 4). This should be compared with the results of the present study, wherein particularly patients who intentionally were treated *without* attempt at removal

Table 4. *Possibility to Remove a Craniopharyngioma Radically. Surgeon's opinion in recent papers* (456 patients)

Reference	Estimated rate of virtual removal, %
Humphreys *et al.* 1979[14]	74
Rougerie 1979[25]	50
Shaphiro *et al.* 1979[27]	58
Laws 1980[17]	64
Carmel *et al.* 1982[11]	33
Patterson and Danylevich 1980[23]	73
Fischer *et al.* 1985[12]	25
Baskin and Wilson 1986[8]	10
Shillito 1986[29]	45
Sorva and Heiskanen 1986[30]	58
Average	49

proved to be in very satisfactory condition at follow-up. Removal of tumour was the aim in $^{15}/_{42}$ cases only and was achieved in $^{10}/_{15}$ (66.6%). This percentage is however deceptive, as in six patients of these ten, the removal was very simple, due to the small size of the tumour.

In the literature, there is the additional difficulty of estimating the real rate of recurrence. Often, a clear distinction is not drawn between a *recurrence* of tumour, in spite of apparently complete removal, and evidence of *continued growth* of tumour remnants, intentionally left at surgery but considered insignificant at that time. The *real failure rate*, i.e. the number of patients *killed by their tumour in a total and long-term perspective* is often difficult to estimate. When various reports are compared, very diverging results may be found. It seems to be, that a minimum of approximately 15% of all patients with craniopharyngioma respond poorly to treatment in the long-term, irrespective of the management programme (cf. Shillito[28]). This should be taken into account, when treatment policies are discussed.

In an outstanding recent article[33], an interesting and very homogeneous material is published; patients operated on by the same surgeon, with uniform technique and with total tumour removal. The authors describe the operation in 20 cases as "removal of all tumour accessible and visible to the surgical microscope". The operative mortality was 5%. During a follow-up of 1.6 to 6.8 years (average 3.1 years), one recurrence was seen (5.5%).

In another very important study[32], highlighting the reality of craniopharyngioma surgery, also by a very experienced surgeon, 40 patients are reviewed: "Of my 37 surviving patients (out of a total of 40 who had a radical operation as the *initial* or *later* operation by me), I have had recurrences in seven ... for an average of 72 months. The 30 patients surviving operation and without recurrence have been followed from 6 months to 31 years, for an average of 12.3 years".

In those patients of the present study who were suitable for exclusive stereotactic treatment (nearly 60% of the total material), the clinical problems related to the progressive growth of the tumour were usually solved by the treatment. It may then be argued, that if the present material is representative of an average population of craniopharyngiomas, nearly 40% would thus be unsuitable for stereotactic treatment. In the present material, however, major surgery could have been avoided in seven patients operated on, and intracystic treatment given, had an improved aspiration technique been used. In more recent cases, it proved possible to aspirate even "porridge-like" cyst contents, using a wider cannula and a "lavage" technique.

More than 20 years ago, Leksell and the senior author of this paper formulated a tentative treatment programme for craniopharyngiomas[19]:

"... first a stereotactic puncture and aspiration for diagnosis. If the tumour is cystic a heavy dose of beta-emitting isotope is injected into the cavity after determining the cyst volume. After obliteration of the cyst cavity residual solid portions of tumor are treated, if necessary, by large doses of stereotaxically directed proton or X-ray irradiation. This technique will also be applied to the primarily solid tumours. Attempts at radical surgical removal will be restricted to the most favourable, small and predominantly intrasellar tumours." The results of the present study do support the tenability of this statement. Stereotactic methods must no longer be disregarded in the management of craniopharyngiomas.

Neurosurgeons less familiar with stereotactic methods may look at such techniques as "competing" alternatives to major surgery, used by special groups only, whereas microsurgical removal is the standard for neurosurgeons in common, *the* method of choice in *any* patient. This is a serious misunderstanding. Both options should be available in any department dealing with these challenging cases, making it possible for the surgeon to individualize the treatment for each patient, *according to the character of the tumour*. When the surgeon is personally familiar with more than one therapeutic alternative, he is able to design the individual treatment programme for each patient with the minimum of bias.

Conclusions

The present study, as well as the experiences reported by others[10, 15, 16, 21, 24, 26, 31], shows that the results obtained with the multi-modality approach used here are not inferior to those obtained when radical microsurgical removal is consistently practized as the first choice. The results indicate, that an optimal management in *any* case of craniopharyngioma should include:

1. *A careful scrutiny of the anatomy of the tumour*, its inner structure in particular, using modern imaging techniques *but also* exploratory stereotactic puncture(s), with the primary aim of disclosing the occurence of cysts, suitable for intracavitary irradiation. A further aim is to determine the proportions between solid and densely calcified tumour parts, soft tissue

areas and cystic compartments, respectively. The clinical "bulk effect" of each of the various tumour components should then be appreciated, as a base for the treatment design. A particular aspect in this context is the fact that neither CT nor MR gives reliable information concerning the proportion between cystic and solid tumour parts, respectively. Craniopharyngioma cysts may have *any* attenuation on CT, and are thus often mistaken for being solid tumours.

2. Stereotactic treatment as the first choice, according to the technique used in the present series, *if* more than approximately 50% of the total bulk of the tumour is cystic and the number of cysts is reasonable, i.e. not more than three.

It is particularly obvious from the present results, that open craniotomy with microsurgical removal of *monocystic* craniopharyngiomas, *especially if they are huge*, may be difficult to justify. In such cases, the non-dramatic, intracavitary treatment induces a safe and permanent obliteration of the tumour. In addition, such treatment makes various shunting/drainage procedures unnecessary, as recommended as a last resort in cases of huge, recurrent cysts[13, 22].

Even though the present material is limited to 42 cases only, it is possible to draw the conclusions reached, due to the relatively long follow-up and the fact that the management protocol has been followed consistently. With few exceptions, one surgeon (E.-O. Backlund) was responsible for the therapeutic decisions.

Since the present material was compiled, the authors have achieved experience from an extensive material. A review of more than 300 patients, including consecutive primary and recurrent cases from 1964 onwards, has recently been initiated. This makes it possible to continue and widen the study, with the aim of seeking the definite principles for optimal craniopharyngioma treatment.

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