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Long Term Results in the Management of Craniopharyngiomas

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The results of surgical treatment, with and without radiotherapy, in 50 patients with craniopharyngioma treated over a 26-year period at the Cleveland Clinic are presented. Thirty-five patients were operated upon before the introduction of the operating microscope, and 30 of these survived operation. In this group of 30 patients, long term survival (5 to 24 years) occurred in 8 of 10 (80%) nonradiated patients who were considered to have had total excision. Nine of 11 patients (82%) who had aggressive subtotal excision and radiation therapy have survived from 3 to 17 years. Seven of nine patients (78%) died 1 to 14 years after subtotal excision without radiation therapy. Since the introduction of the operating microscope in 1972, 15 patients have had surgical treatment, and 12 of these have survived.

Key words: Craniopharyngioma, Long term survival, Radiation therapy, Cyst aspiration

INTRODUCTION

There is unresolved controversy regarding the optimal treatment of craniopharyngiomas. Of particular concern are the necessity for complete surgical excision and the role of postoperative radiation therapy. We have attempted to answer some of these questions by a retrospective analysis of patients treated during a 26-year period at the Cleveland Clinic.

The longest surviving patients in this series are those treated with either total tumor removal or with radiation after subtotal removal. Very poor survival has occurred in patients treated with subtotal removal only.

Long term survival after entirely surgical treatment in other series has not always been satisfactory. Furthermore, there is strong evidence to indicate that radiation improves the results of surgical treatment. These subjects are reviewed in the discussion.

CLINICAL MATERIAL

Between 1950 and 1976, 50 patients were treated surgically by various members of the neurosurgical staff of the Cleveland Clinic. There were 35 adults (18 years or older) and 15 children.

All but two of these patients received their first operation at the Cleveland Clinic. The surgical approach in most cases was transfrontal or subtemporal, more frequently from the right side, although a left or bifrontal approach was used in cases involving the extension of the tumor primarily to the left side. In two cases the tumor was totally excised *via* a trans-sphenoidal approach. Trans-sphenoidal marsupialization of a large recurrent cyst was carried out in one case. Transcortical approaches were used in four selected cases.

The periods of survival represent minimum periods of survival based on the most current information available. Four patients were lost to follow-up; one in 1958, one in 1964, and two in 1970. Information concerning the other patients is current to within less than 3 years of this report except for three cases.

Ten of the 50 patients had more than one craniotomy, including two patients operated upon elsewhere prior to treatment at the Cleveland Clinic. Six of the reoperated patients died. Three of the four who survived are blind, although two of the survivors have had good quality survival.

Total removal was not possible in 33 of 50 cases, usually because of adherence of the tumor to optic structures, the hypothalamus, or the carotid artery.

Unfortunately, incomplete data exist regarding the method and exact amount of radiation therapy due to the fact that some of the patients were treated at other centers. Where the radiation dose is known, the amount of ^{60}Co irradiation delivered to the tumor site ranged from 4500 to 5500 rads in most cases before about 1973. Patients treated more recently received 5700 to 6000 rads *via* multiple ports. One early patient received only 2250 rads and had a poor result. Treatment in another patient was discontinued after 1600 rads due to failing vision.

CLINICAL FEATURES

The presenting symptoms are noted in Table 1. Decreased vision was most common (35 patients), followed by headache (25 patients). Symptoms of hypogonadism (14 patients), polyuria (11 patients), and appetite disturbance (6 patients) were also noted. One patient had galactorrhea. Seven adult patients were demented. Five patients, including four children, presented with an altered level of consciousness. More than one-half of the children were of short stature.

The preoperative visual fields available in 30 patients are noted in Table 2. Fifteen patients had an incongruous field deficit, seven had bitemporal hemianopsia, four had homonymous hemianopsia, three had normal vision, and one patient was totally blind.

Preoperative endocrine studies were incomplete, but indicated that most patients tested had gonadotropin deficiency (Table 3). Twenty-two per cent of the 50 patients had diabetes insipidus.

RESULTS

The over-all survival for 50 children and adults with total and subtotal excision is depicted in Table 4. Some period of good quality survival was experienced by about 60% of the patients, irrespective of whether removal was total or subtotal.

It is too early to comment about the influence of the operative microscope on the treatment of craniopharyngiomas except to state that 12 of 15 patients (80%) operated upon with the aid of the microscope are alive and that 9 of the 15 patients (60%) had a subtotal removal. These patients received radiation therapy.

Thirty-five patients were operated upon without the microscope. Figures 1 and 2 illustrate the survival times in the 30 patients who survived the immediate postoperative period from this group. In viewing these illustrations, three groups seem to stand out. Two groups of living patients with

TABLE 1
Craniopharyngioma: Presenting Symptoms among 50 Patients

Symptom	Adults (35)	Children (15)	Total Patients	
			No.	%
Decreased vision	25	10	35	70
Headache	15	10	25	50
Endocrine abnormalities				
Amenorrhea/impotence	13	1	14	28
Polyuria	6	5	11	22
Appetite disturbance	5	1	6	12
Galactorrhea	1	–	1	2
Altered mentation				
Dementia	7	–	7	14
Altered level of consciousness	1	4	5	10
Short stature	–	8	8	16

TABLE 2
Craniopharyngioma: Preoperative Visual Field Testing

Result	No. Patients	%
Incongruous deficit	15	50
Bitemporal hemianopsia	7	23
Homonymous hemianopsia	4	13
Normal, both eyes	3	10
Blindness, both eyes	1	3
Total	30	100

TABLE 3
Craniopharyngioma: Preoperative Endocrine Status

Endocrine Deficit	Patients Tested	% with Deficiency
Gonadotropins	15	93
Follicle-stimulating hormone	5	80
Cortisol	10	78
17-Hydroxycorticosteroids	10	70
Luteinizing hormone	7	67
17-Ketosteroids	10	60
Thyroid hormone	15	38
Growth hormone	6	33
Diabetes insipidus	50	22

TABLE 4
Craniopharyngioma: Survivors in 1976 from Surgery Performed 1950–1976

	Alive		Dead	
	No.	%	No.	%
Adults *vs.* children				
Adults	20	57	15	43
Children	8	53	7	47
Type of operation*				
T/M	4	67	2	33
T/NM	6	55	5	45
ST/M	7	78	2	22
ST/NM	11	46	13	54
Total	28	56	22	44

* T, total excision; ST, subtotal excision; M, microscope used; NM, no microscope used.

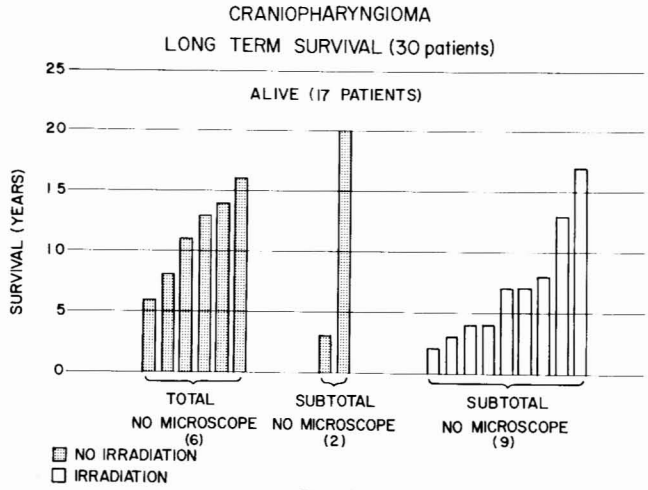

FIG. 1.

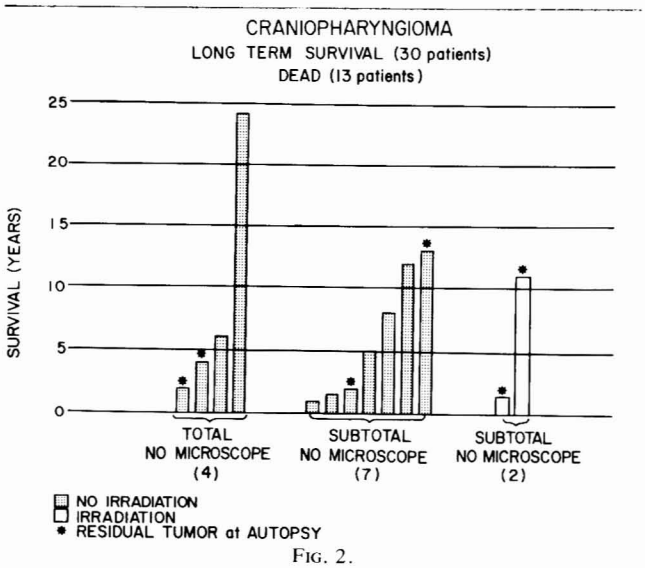

FIG. 2.

relatively long survival are seen in Figure 1. The first of these is a group of nonradiated surviving patients; most of these individuals had total tumor removal. A second group of irradiated patients who had subtotal excision continue to survive 3 to 17 years after surgery. The third group is depicted in Figure 2. These patients are all dead, and most did not receive radiation therapy, the two exceptions having received 1600 and less than 2250 rads, respectively. The tumor excision was subtotal in 9 of the 13 cases. The only long term survivor (24 years) in the third group had a total excision.

Early postoperative deaths were due to operative trauma or hemorrhage; later deaths were largely related to tumor recurrence (Table 5). Nine of 11 patients examined postmortem had residual tumor. Tumor was found in two of three patients autopsied after "total removal."

Of the 15 children in the series, 7 are dead (47%). Six children (40%) survive after subtotal removal plus irradiation. Four of five children in whom total removal was accomplished are dead. Of the longest surviving children, one has been followed 7 years and the other 17 years.

CASE REPORTS

Of interest in this series are two patients who were treated with repeated cyst aspiration and radiation therapy in the face of recurrent clinical deterioration.

Case 1

This 7-year-old boy presented in April 1959 with headache of 6 months' duration, right homonymous hemianopsia and a right 6th cranial nerve palsy of 1 week's duration, and lethargy of 3 days' duration. He underwent subtotal removal of a cystic craniopharyngioma *via* a left frontal craniotomy; remnants of tumor were left on the left carotid artery, left 3rd cranial nerve, and left optic nerve.

Due to repeated episodes of headache, lethargy, and failing vision, five separate transventricular aspirations of cystic contents were performed in June 1962. On each occasion, 45 to 80 ml of dark fluid were aspirated.

In June 1962, 5500 rads of ^{60}Co were directed to the site of the tumor with resultant termination of cyst formation. His vision remained severely restricted in both eyes.

The patient was reoperated upon in 1974 due to sudden loss of vision after a minor head injury; adhesions were encountered in the region of the optic nerves, and beneath the adhesions was a dense, calcified area to which they were firmly attached and which contained less than 3 ml of viscous, turbid fluid. Only light perception returned. He is presently alive and working at age 25 years. He receives replacement endocrine treatment for panhypopituitarism.

TABLE 5
Craniopharyngioma: Causes of Death (0 to 24 Years Postoperatively)

Cause	No. Patients	%
Postoperative		32
Hemorrhage	3	
Coma from operative trauma	4	
Tumor recurrence		54
Verified	9	
Suspected	3	
Other		14
Adrenal failure	1	
Co-existing CLL*	1	
Unknown	1	
Total	22	100

* Chronic lymphocytic leukemia.

Case 2

This man presented on February 24, 1973, when he was 32 years old, with an 8-month history of progressive anterior hypopituitarism, diabetes insipidus, and constricted visual fields with bitemporal hemianopsia. At the time of admission, he had obstructive hydrocephalus due to a suprasellar tumor.

A right frontal craniotomy was performed on March 2, 1973. The tumor, a largely solid craniopharyngioma with a cystic component, presented as an infrachiasmatic mass and was excised totally through a lateral approach between the right carotid artery and the right optic nerve. A large suprasellar collection of xanthochromic fluid was removed on May 16, 1973. On May 18, 1973, further headache and decreased vision occurred, and a similar collection of fluid was aspirated.

Percutaneous aspiration was again carried out on July 23, 1973, and ^{60}Co radiation therapy was instituted. Shortly after the start of treatment, reaspiration was again necessary for the same reasons. The radiation therapy was interrupted, but eventually was completed. A final aspiration was performed on February 15, 1974, after which the patient's vision again improved. A pneumoencephalogram performed on March 26, 1974, did not demonstrate a mass. A computerized tomographic (CT) scan on April 16, 1975, was normal. Ophthalmological examination in May 1975 revealed visual acuity O.D. 20/30, O.S. 20/20, with a bitemporal visual field deficit. The patient has not returned to work.

DISCUSSION

Craniopharyngiomas are unusual tumors constituting 1.76% of 6135 brain tumors in Olivecrona's series as reported by Svolos (14). Of 758 hypophyseal and parahypophyseal tumors in the same series, 14% were craniopharyngiomas, 68% were pituitary adenomas, and 11% were suprasellar meningiomas. Other less common lesions collectively constituted 7% of the same series.

The natural history of these tumors is highly variable. Bartlett (1) reported three patients who were followed more than 25 years without any form of treatment. He also followed three patients who developed recurrence of tumor at 15, 20, and 21 years after total excision. Most patients become symptomatic, and patients of all ages are subject to manifestations of the disease. The duration of symptoms is variable, being less than 3 years in 50% of the afflicted patients, but up to 30 years in others. Visual and endocrine abnormalities are commonly present. Hydrocephalus is common in children. Dementia may be the dominant presenting feature in adults. The clinical analyses of Love and Marshall (10), Svolos (14), Pertuiset (13), and Hankenson and Banna (4) discuss this subject thoroughly. Pertuiset (13) gives a particularly good review of the technical considerations of importance in the treatment of these tumors.

When feasible, total excision is the ideal method of surgical treatment. According to Katz (7), this principle was established by Matson, who accomplished what he considered to be total removal in 34 of 51 children operated upon for craniopharyngioma. Katz (7) reports that nine (26%) of these patients developed tumor recurrence and three died without evidence of tumor recurrence. Thus, 25 of 34 patients (74%) were considered to be cured of the tumor, and 22 of these 34 patients (65%) are living without evidence of recurrence.

Unfortunately, total removal is not always possible, and lóng term survival after entirely surgical treatment is not always satisfactory. Among the largest neurosurgical series in the poststeroid era, useful survival after operation without irradiation is reported as follows: Northfield (12), 16%; McKissock and Ford (11), 22%; Svolos (14), 19%; Hoff and Patterson (5), 25%; and Kahn *et al.* (6), 21% of children and 67% of adults.

An early report by Carpenter, Chamberlin, and Frazier (3) concerning long term survival after aspiration and irradiation of craniopharyngiomas in four patients is one of the first indications of the usefulness of radiation therapy in the management of craniopharyngiomas. Leddy and Marshall (9) reported 10 cases in which remission or improvement of symptoms occurred with postoperative radiation therapy. McKissock and Ford (11) reported that 73% of 45 patients were alive and working after combined radiation and surgical treatment, in contrast to 22% of 55 surgically treated patients. Kramer, Southard, and Mansfield (8) reported long term survival of good quality in 70% of 26 patients after aggressive, technically localized radiation therapy after generally conservative surgical procedures. Bartlett (1) reported one patient who survived 29 years with remission of symptoms due to a craniopharyngioma. This patient was operated upon and also received radiation when he had symptoms of tumor recurrence soon after the operation. Hoff and Patterson (5) reported that evidence of recurrence existed in 89% after resection only and in 63% after resection plus radiation therapy. Bloom (2) reported that 61% of 33 patients were alive 10 years after conservative surgery combined with aggressive radiation therapy.

Other less well established methods of radiation therapy are reviewed by Pertuiset (13). These primarily involve the introduction of various isotopes directly into the cyst cavity. None of the patients in the present series has been treated with these methods.

CONCLUSION

We agree that total excision is the ideal method of treatment, but in those instances when this cannot be done safely subtotal removal combined with radiation therapy is an acceptable alternative.

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COMMENTS

The authors present a realistic picture of their experience with a difficult condition as treated at a major neurosurgical clinic. They substantiate the importance of treatment of craniopharyngioma with radiotherapy, especially when removal is incomplete. It is valuable to have this documentation of the over-all results that can be obtained in a large series of patients. The paper also gives a good review of previous literature on the subject.

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This paper substantiates the desirability of total excision of craniopharyngiomas first advocated by Donald Matson. But when radical removal is unwise, the authors show good clinical results when subtotal removal is followed by well directed radiotherapy. Similar observations have been made before, but this paper provides additional evidence for the value of a flexible approach to craniopharyngiomas, even in the era of the operating microscope. Case 1 is of particular interest, strongly implying that craniopharyngiomas are "curable" even if they are not totally removed at operation.

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