Management of craniopharyngioma in children


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The authors reviewed 48 cases of craniopharyngioma in children treated during 25 years, 1950 to 1975. Complete excision of the tumor, attempted in 23 patients, was possible in 17. The authors advocate aggressive treatment aimed at complete excision of the tumor, using radiotherapy only when adherence of the tumor to the internal carotid artery precludes total excision, and symptoms recur.

KEY WORDS • craniopharyngioma • aspiration • subtotal excision • total excision • radiotherapy • visual defects • endocrine symptoms

Craniopharyngiomas primarily develop during childhood and are the commonest intracranial tumor of nonglial origin in children; in Matson’s clinic in Boston, they accounted for 9% of all intracranial tumors in children.11 These neoplasms are thought to arise from embryonic squamous-cell rests of an incompletely involuted hypophyseal pharyngeal duct. The rests, which are in the pituitary stalk and infundibulum, can develop into tumors of squamous epithelium, growing slowly and encroaching on surrounding structures. In the vast majority of cases, degeneration products cause cystic changes in the center of the tumor (Fig. 1).

Treatment of these tumors is controversial. The panhypopituitarism provoked by removal of these tumors led Cushing to say that craniopharyngiomas “offer the most baffling problem which confronts the neurosurgeon,”14 but the outlook has changed since the advent of steroid replacement therapy. In 1950, Matson began to attempt complete removal of every craniopharyngioma.12 The operative mortality was nil, and a 1975 review of his cases revealed that the tumor had not recurred in 53%.7 Other surgeons, however, have been less successful in treating craniopharyngiomas in childhood. Complete excision was achieved by Hoff and Patterson5 in only two (12.5%) of 16 cases and by Kahn, et al.,8 in 32%. Bartlett1 stated that total removal of a craniopharyngioma was impossible and that radical excision was possible in only 6% of cases. Kahn, et al.,6 found tumor recurrence after what had appeared to be complete excision, and stated that they could classify the result as good to excellent in only 21% of their children.

Kempe6 has stated emphatically that the capsule of a craniopharyngioma is closely attached to the hypothalamus and that attempting complete removal of the tumor...
Craniopharyngiomas in children

Fig. 1. Stages of development of craniopharyngioma from squamous-cell rests shown by diagrams of coronal section viewed posteriorly. ICA = internal carotid artery, LV = lateral ventricle, M = pia arachnoid, OT = optic tract, P = pituitary gland, S = pituitary stalk, SCR = squamous cell rests, T = craniopharyngioma, TV = third ventricle.

Invariably leads to infarction of the hypothalamus. He therefore advocates never trying to remove the tumor capsule posteriorly and superiorly, considering the objective of the operation to be reduction of the tumor mass rather than its removal. Similarly, Kramer, et al.,9 and Bloom3 have emphasized that complete excision of a craniopharyngioma is difficult in all cases and impossible in some, and carries an extremely high operative mortality. They recommend simple decompression of the tumor cyst followed by radiotherapy, a course of action favored by many radiotherapists and neurosurgeons.

In recent years, better endocrinological management of these patients, combined with use of the operating microscope, has reduced the operative mortality and permitted a much higher incidence of complete excision of these tumors. We have compared the experience at our institution of radiotherapy after simple decompression with complete excision of the tumor.

Clinical Material and Methods

During the years 1950 to 1975, 48 children (24 of each sex) underwent surgery for craniopharyngioma; 17 were 2 to 6 years of age and 31 were aged 7 to 16 years. All but one had visual defects: papilledema was present in 13, bitemporal hemianopia in 25, homonymous hemianopia in four, and unilateral temporal hemianopia in four; visual acuity was significantly reduced unilaterally in 17 and bilaterally in 11; see-saw nystagmus was present in three cases.

More than 50% of the patients had endocrine symptoms: six had diabetes insipidus, nine were excessively short, seven were excessively obese, two were hypothyroid, and four showed evidence of sex-hormone deficiency. Plain skull radiographs revealed calcification within the tumor in 29 patients. In seven cases, severe hydrocephalus produced by the tumor necessitated shunting before the craniopharyngioma could be dealt with surgically.

Primary surgical treatment consisted of aspiration of the tumor contents in 16 cases, subtotal extirpation of the tumor in 15, and its complete removal in 17. Sixteen of the children received radiotherapy at some time. In the five patients treated early in the series, irradiation was with cobalt-60 gamma rays, using a three- or four-field beam-directed method with a plaster cast. The other 11 patients were treated in a cast with a betatron, using parallel opposed 22-MeV x-rays, which is still our standard technique. The field size varied from 6 × 6 to 10 × 10 cm (median, 8 × 8 cm), and the total dose (1000 rads per week in five equal fractions) varied from 4225 to 5900 rads (median, 5250 rads).

Summary of Cases

Treatment by Aspiration

In 16 cases the tumor was treated by cyst aspiration, biopsy, or partial tumor removal (Fig. 2). In all of these patients, recurrence of the tumor necessitated repeat craniotomies for aspiration or further excision of the
FIG. 2. Graph shows clinical course and outcome in 16 cases of craniopharyngioma treated initially by aspiration, biopsy, or partial removal of the tumor.

FIG. 3. Lateral skull radiographs of Case 1 (see Fig. 2). Left: At the initial presentation, aged 2 years. Right: Shortly before death, at the age of 15 years, after multiple operative procedures and one course of radiotherapy; there is massive residual tumor.
Craniopharyngiomas in children

TABLE 1
Neurological, visual, and endocrine function in 48 children after treatment for craniopharyngioma

<table>
<thead>
<tr>
<th>Postoperative Status</th>
<th>Aspiration, Biopsy, or Partial Removal</th>
<th>Subtotal Excision</th>
<th>Total Excision</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal CNS function, intelligence &amp; visual acuity</td>
<td>1</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>normal CNS function, intelligence &amp; visual acuity; visual field defect</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>normal CNS function &amp; intelligence; mild loss of visual acuity</td>
<td>2</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>normal CNS function &amp; intelligence; moderate or severe loss of visual acuity</td>
<td>3</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>mild neurological deficit; normal intelligence, severe loss of visual acuity</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>comatose vegetative state</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>improved visual acuity</td>
<td>1</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>endocrine status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>diabetes insipidus</td>
<td>4</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>treated with cortisone</td>
<td>3</td>
<td>7</td>
<td>11</td>
</tr>
<tr>
<td>treated with thyroid</td>
<td>3</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>treated with sex hormone</td>
<td>3</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>normal growth</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>survivors</td>
<td>6</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>total patients</td>
<td>16</td>
<td>15</td>
<td>17</td>
</tr>
</tbody>
</table>

tumor. Three of eight patients with shunts in this group required multiple shunt revisions; one required six.

Ten patients received radiotherapy, two as prophylaxis after the initial minimal attack on the tumor, and the other eight as treatment of tumor relapse. Both of the former and three of the latter died. At the time of death, all five had significant tumor masses; two of these also had intercurrent infections and were not protected with cortisone. Two patients received no radiotherapy until multiple operative procedures had been performed over several years; both survived for several years after irradiation. Radiographs of one of these patients are shown in Fig. 3.

In all 16 cases the tumor recurred after initial treatment; 10 of these patients have died (Table 1). One of the six survivors is well 16 years after initial treatment and without irradiation; the others are still alive 11 years (two patients), 9 years (one patient), and 3 years (two patients) after initial treatment. One has better vision now than before treatment and one has normal vision; four have diabetes insipidus. Three patients are being treated with cortisone, three with thyroid, and three with sex hormones, and one is growing normally without exogenous growth hormone.

Subtotal Resection of Tumor

Subtotal surgical resection of the tumor was performed in 15 cases (Fig. 4). The surgeon either considered that he had removed virtually all the tumor, leaving only that which was adherent to important structures, or strongly doubted that he had removed all of the tumor. In fact, complete excision was attempted in only six cases, and it was considered that adherence of the tumor to the internal carotid artery made this impossible; in the other nine cases, the surgeon considered total excision impossible and did not attempt complete removal. Only two of these 15 patients have died, in both cases 3 years after initial treatment and due to tumor recurrence; neither had received radiotherapy.

Six patients have had a repeat craniotomy because of tumor recurrence; only one has had more than two intracranial operations. A shunt was inserted before resection in one patient, and hydrocephalus due to recurrent tumor developed after resection in another; neither has required shunt revision.
Six patients were irradiated because of tumor recurrence. One of these (Case 1, Fig. 4) received radiotherapy after a second subtotal excision 5 years after the first one; he has had no further operative treatment and remains well 2½ years later. Four patients underwent an aspiration procedure, followed by prophylactic radiotherapy, because of the recurrence of symptoms after subtotal resection; only one required repeat aspiration, which was performed 3 months after the course of radiotherapy. One patient (Case 13, Fig. 4) developed recurrent symptoms 10 months after his initial subtotal resection. He was irradiated then without further operative intervention and remains well 2 years later. All six patients are well, three of them 8 years and the other three more than 2 years since radiotherapy.

The other seven survivors, who were not irradiated, have no evidence of tumor recurrence and have undergone no further intracranial procedures. They are now well 1 year after subtotal resection (two patients), 2 years (one), 3 years (two), 6 years (one), and 20 years (one). In this last case, an air study done 19 years after the radical excision was perfectly normal, showing no evidence of recurrent tumor.

Six of the 13 survivors (Table 1) have better vision now than before treatment; two have normal vision. Seven patients have diabetes insipidus; seven are being treated with cortisone, 11 with thyroid, and five with sex hormones, and one appears to be growing normally without exogenous growth hormone.

**Total Excision**

In 17 patients the entire tumor was removed (Fig. 5); radiotherapy was not given. None has required further surgery for tumor

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**PATIENTS**

![Graph showing clinical course and outcome in 15 cases of craniopharyngioma treated initially by subtotal excision of the tumor.

**YEARS**

- **ASPIRATION**
- **SHUNT**
- **RADIOThERAPY**
- **SUBTOTAL EXCISION**
- **DEATH**

**SUBTOTAL EXCISION**

**Fig. 4.** Graph shows clinical course and outcome in 15 cases of craniopharyngioma treated initially by subtotal excision of the tumor.
Craniopharyngiomas in children

PATIENTS

![Graph showing clinical course and outcome in 17 cases of craniopharyngioma treated initially by total excision of the tumor.]

Fig. 5. Graph shows clinical course and outcome in 17 cases of craniopharyngioma treated initially by total excision of the tumor.

Of the 15 patients still alive (Table 1), eight have survived for 1 to 4 years, six for 6 to 11 years, and one for 12 years. Vision has improved in 10, to normal acuity and fields in five. Fourteen patients have diabetes insipidus, 11 are being treated with cortisone, 13 with thyroid, and four with sex hormones, and three are growing normally without growth-hormone therapy.

**Discussion**

**Comparison of Methods of Treatment**

Comparison of the results obtained in our three groups of patients is shown in Table 1. In our comparisons, we defined mild visual loss as decreased vision with acuity 20/40 or

recurrence, and none of the three who had shunts inserted preoperatively has required shunt revision or additional shunting.

Two patients died, one immediately postoperatively (in 1955, before introduction of the operating microscope). The other remained well for 2 years, but hypoglycemia developed during a metopyrone test in another institution and death ensued. There have been two operative catastrophes: in addition to the one death, massive cerebral infarction developed in a patient treated more recently (also without the operating microscope) and she remains comatose. All of the eight patients who had the benefit of microsurgical total excision of their tumor experienced no operative morbidity and are alive.
Fig. 6. Craniopharyngiomas found at autopsy of two children who died before any treatment had been given; coronal section (upper); sagittal section (lower). In both cases the tumor was adherent to the tuber cinereum only.

better bilaterally, moderate visual loss as acuity less than 20/40 in one eye, and severe visual loss as acuity less than 20/40 bilaterally.

Aspiration, even when prophylactic radiotherapy was used, was followed by tumor recurrence in all 16 patients; the mortality rate was 62.5%. When subtotal excision was performed, only 53% of the tumors recurred and the mortality rate dropped to 13.3%. With total excision, the recurrence rate was zero and the overall mortality rate was 11.8%; in the eight patients in whom total microsurgical removal was performed, both mortality and operative morbidity were nil. The patients whose tumors were completely excised have also done better functionally. Whereas vision and neurological function are normal in only one of the six survivors treated by aspiration, and in only two treated by subtotal resection, both are normal in five of the 15 survivors treated by total excision. Vision improved in only one patient who had aspiration only, in six who had subtotal excision, and in 10 who had total excision of the tumor.

Obviously, during total removal of these tumors the median eminence of the hypothalamus is almost invariably damaged. Diabetes insipidus has developed in 14 of the 15 survivors who had a total excision but in only seven of the 13 survivors who had a subtotal excision and four of the six treated by aspiration. Other endocrine functions are similarly impaired in both of the latter groups, but normal growth without growth-hormone therapy appeared more common after total excision.

Further treatment was required for recurrence of symptoms in every patient treated by aspiration, biopsy, or partial removal, but in only eight of the 15 in whom subtotal resection was performed. Seven of the latter patients have not had a recurrence of their symptoms and have not received radiotherapy. Of the eight with recurrence, two died after their second operative intervention and six were irradiated, without operative intervention in one, and after a second operation in five.

Eleven of the 16 irradiated patients are still alive. Of those in whom subtotal excision was the treatment of choice, all six patients who received radiotherapy for recurrent symptoms are functionally well. Of the 10 patients who were irradiated after aspiration initially, five are dead.

The formation of cyst fluid was controlled in some cases. Three of the 16 irradiated patients had symptomatic re-accumulation of fluid within 1 to 3 months after therapy: this was controlled by repeat aspiration in two cases and by subtotal tumor excision in one. This last patient died at home during an infectious illness and autopsy revealed a large residual tumor.

Possibility of Total Excision

Since craniopharyngiomas arise from squamous-cell rests within the pituitary stalk or infundibulum, the tumor is closely adherent to a small portion of the floor of the third ventricle in the area of the tuber cinereum. Elsewhere, it is covered with meninges and is completely free of the remainder of the hypothalamus, the basilar artery, and the brain stem. Unless it has been treated previously, the tumor can usually be freed relatively easily from the optic nerves, optic chiasm, and optic tracts. We have examined pathological specimens of craniopharyngiomas removed at autopsy from two children who died shortly after admission to
Craniopharyngiomas in children

FIG. 7. Macroscopic appearance of craniopharyngioma at autopsy (Case 10, Fig. 2), showing dense adherence to brain. Previous manipulation of the tumor (aspiration and radiotherapy) has apparently “cemented” the tumor into hypothalamic tissue.

this institution over 30 years ago. In neither specimen was the tumor capsule adherent to the brain stem or basilar artery posteriorly; there was a small area of adherence to the tuber cinereum, but the tumor was free of the optic apparatus and internal carotid artery (Fig. 6). At operation, the only site of tumor adherence we have found that prevented total excision was between tumor and internal carotid artery. However, previous manipulation of a tumor, surgically or by irradiation, produces such dense adhesions that the tumor capsule becomes firmly adherent to contiguous structures and curative surgery is not possible (Fig. 7).

The entire tumor was removed in 17 of the 23 patients in whom this was attempted, indicating that complete removal is possible in approximately 74% of cases. Furthermore, three of the six unsuccessful attempts at total excision were without benefit of an operating microscope; had this been available, magnification might have permitted complete excision. Neither the size of the tumor nor the age of the child appeared to affect the possibility of total excision.

As Northfield has pointed out, the possibility of total excision of craniopharyngiomas in children and in adults may be quite different, since in the latter the leakage of cyst fluid for many years is likely to have created dense adhesions. Muller, et al., were also unable to excise completely 29 of 31 craniopharyngiomas in adults, but they did achieve good results without radiotherapy, despite recurrent symptoms in two-thirds of their patients.

Operative Approach for Total Excision

The tumors are approached subfrontally through a large right frontal flap; if the tumor extends behind the clivus, the temporal lobe is retracted. After exposure of the tumor, a needle is inserted into the tumor and the cyst is aspirated (typical craniopharyngioma cysts contain cholesterol crystals, which glisten in bright light). The capsule is incised and the tumor is gutted.

Tumor attachments to the optic apparatus, internal carotid artery and hypothalamus are dissected with the aid of the operating microscope, after which it is usually relatively easy to pull the tumor loose from surrounding structures. The tumor is usually delivered between the optic nerves; if the chiasm is prefixed, the lamina terminalis is incised and the tumor is rocked between its suprasellar attachment and the opening in the lamina terminalis. With the latter maneuver, some portions of the tumor can be delivered through the lamina terminalis and some between the optic nerves (Fig. 8).

Bergland and Ray have demonstrated that the blood supply of the optic chiasm is derived from an inferior group of vessels arising from the internal carotid artery, the posterior cerebral artery, and the posterior communicating artery. With the aid of the operating microscope, it is usually a simple matter to separate the capsule of the craniopharyngioma from this inferior group of vessels and thus avoid producing ischemia of the chiasm and optic tracts. Only rarely is the capsule densely adherent to the optic tracts. In such cases it is possible to free the capsule but there is risk of compromising the vascular supply, which can lead to deterioration of visual acuity. In those patients treated by a microsurgical total excision, we have not seen deterioration in vision, and in fact vision has improved in the majority of patients treated by total excision. On the other hand, if one leaves portions of the tumor adherent to the chiasm, there is risk of progressive ischemia of this structure and progressive loss of vision.

Bergland and Ray have pointed out that the optic apparatus is also supplied by a
in patients with craniopharyngiomas was related more to compression of the vascular supply to the optic chiasm than to distortion of the chiasm by the tumor. This seems to be borne out by our group of patients in that 10 of the 15 who had a total excision of their tumor have had improvement in their vision whereas, where tumor was left behind, even though the chiasm was decompressed, improvement in vision was far less frequent, occurring in only one of the six patients treated by aspiration, and in six of 15 treated by subtotal excision.

**Irradiation Therapy**

Although radiotherapy doubtless decreases cyst fluid formation, it probably does not destroy craniopharyngioma epithelium; in several of our patients whose symptoms were controlled by radiotherapy, computerized tomography (CT) scans have shown large tumor masses. Radiotherapy does, however, cause degenerative changes in brain parenchyma and vasculature (Fig. 9); the changes induced by a dose of 5000 rads in 5 weeks will progress slowly over a time scale measured in decades, resulting in an increased incidence of vascular catastrophes in later years and enhancing the possibility of tumors within the irradiated volume. The risk of tumor induction by irradiation in a young child with a benign lesion can be significant; Waga and Handa recently reported the development of meningioma in a patient thus treated for a craniopharyngioma.

**Conclusions**

Total excision of a craniopharyngioma in childhood is possible and, with the aid of an operating microscope, can be carried out without surgical morbidity or mortality. This is the treatment of choice in this age group, with the expectation of cure of the tumor, prevention of recurrence, and avoidance of the side effects of radiotherapy. Fear of inducing diabetes insipidus should not influence a surgeon’s decision to attempt complete extirpation of the tumor; this easily managed endocrine problem is negligible in comparison with the possibility of tumor recurrence. An additional benefit of complete excision of the tumor is the apparently greater likelihood of the child’s normal growth without exogenous growth hormone.
Craniopharyngiomas in children

an effect for which we have no explanation. In those few cases where tumor adherence to the internal carotid artery prevents total excision, one should wait for evidence of tumor recurrence before subjecting a patient to radiotherapy. These patients can be followed with CT scans, and only if there is unequivocal evidence of a recurrent suprasellar mass lesion should irradiation be undertaken.

In conclusion, we consider Matson and Crigler’s thesis that complete removal of craniopharyngiomas is possible in children has been vindicated by the long-term results in their own cases and by the present series.

Acknowledgments

We thank Drs. W. S. Keith, J. D. Bailey, R. E. Ehrlich, and N. Howard for allowing us to study their patients.

References


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