Aggressive surgical management of craniopharyngiomas in children

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The cases of 50 patients with craniopharyngioma operated on at The Hospital for Sick Children in Toronto between January, 1975, and December, 1989, are reviewed. All patients were under 18 years of age (mean 9.39 years). Headaches, endocrine deficiencies, and visual deficits were the most common symptoms on admission. Forty-five patients underwent what was considered by the surgeon to be total excision of their tumor, and five had subtotal excision. Tumors recurred in 17 patients (mean time of recurrence 32.6 months after surgery). One patient died in the postoperative period and three have been lost to follow-up study. Of the remaining 46 patients, 28 are leading a normal or nearly normal life, although all are receiving endocrine replacement and some have required help to overcome mild deficits in memory or visual acuity. Twelve patients are able to function reasonably well and attend school despite being hampered by intellectual or visual deficits or problems with weight control; four have a significant handicap, and two have died.

KEY WORDS • craniopharyngioma • diabetes insipidus • endocrine dysfunction • hydrocephalus • radiation therapy

CRANIOPHARYNGIOMAS, which are primarily tumors of childhood, are the most common intracranial tumor of nonglial origin in children. Their treatment has always presented a challenge to the neurosurgeon. Despite the benign histological appearance of these tumors, many patients demonstrate a progressively deteriorating course, regardless of therapy, and die of their disease.7 The method of managing these tumors remains controversial; proponents of radical removal, radiation therapy, or a combination of these modalities vigorously espouse their points of view.1,2,4,6,8-17,19,20,22,26 During a 15-year period from 1975 through 1989, total excision of the craniopharyngioma was the primary goal of treatment at The Hospital for Sick Children.

Clinical Material and Methods

Case Selection
The charts of all patients admitted to The Hospital for Sick Children between January 1, 1975, and December 31, 1989, and diagnosed as having craniopharyngioma were reviewed. A total of 93 patients underwent surgical management of their craniopharyngioma during that period. For the purpose of this review we selected patients whose first microsurgical tumor removal was performed at this hospital. Fifty of the 93 patients fulfilled this criterion. Their charts were reviewed for age, sex, presenting symptoms, treatment, results of neuroimaging, tumor recurrence, results of neuropsychological tests, and data obtained at the last available follow-up examination. Whenever possible, the children were brought back to the hospital for complete clinical examination, neuroimaging, and neuropsychological tests. When this was not possible, the referring physician was contacted to obtain adequate follow-up data.

Statistical analysis of the data was performed. Kaplan-Meier actuarial survival curves and log logistic regression modeling were used to study the recurrence-free intervals and the probability of tumor recurrence in relation to preoperative variables.

Presenting Characteristics

Age and Sex. The study included 22 girls and 28 boys whose age at the time of surgery ranged between...
1 year 10 months and 17 years 7 months (mean 9.39 years). Twenty-one patients (42%) were between 8 and 12 years of age.

**Symptoms.** Headache, the most common complaint on admission, was present in 34 (68%) of the 50 children. Its duration could be ascertained in 25 patients and ranged from 2 weeks to 4 years (mean 37.8 weeks).

Symptoms or signs related to the endocrine system were very common, being present in 33 patients (66%). Seven patients were hypothyroid as detected by preoperative screening tests (thyroxine < 5 μg/dl), with normal or low level of thyroid-stimulating hormone. Twenty patients were of short stature; at admission, this was either the major complaint or height was found to be below the third percentile of their age and sex. Twelve patients had diabetes insipidus at admission. Nine patients were obese, with weights above the 97th percentile for age and sex or with a history of recent excessive weight gain. Seven children displayed a delay in the appearance of secondary sexual characteristics, and one presented with precocious puberty at the age of 5 years.

Complaints relating to vision were present in 29 children (58%). Nineteen had a field defect, the most common being a bitemporal hemianopsia (eight patients). Twenty-one children had decreased visual acuity in one or both eyes; four were blind in one eye. Four children complained of diplopia and two had seesaw nystagmus. Visual acuity showed a very significant relationship to tumor location. Of the 25 patients with a prechiasmatic tumor, 15 (60%) had a defect in visual acuity and 14 of them suffered a severe loss of vision (visual acuity < 20/60); 12 (48%) of these 25 children had a visual field defect. Of the 23 patients with a retrochiasmatic tumor, five (21.7%) had impaired visual acuity and seven (30.4%) had a visual field defect. The two patients with sellar tumors had normal acuity and normal visual fields.

**Neuroimaging Examination**

All of the patients underwent computerized tomography (CT) and those treated during the past 5 years underwent magnetic resonance (MR) imaging as well. We found evidence of tumor calcification in all 50 patients. The calcification was usually particulate and could be extensive; occasionally it was massive and bone-like in appearance. The tumors usually contained some form of cyst formation, frequently large (Fig. 1). In 10 patients (20%) the tumors were solid without cyst formation. Some degree of sellar enlargement and/or blunting of the dorsum sellae was noted in 20 patients (40%).

Twenty-five patients (50%) had prechiasmatic tumors. These protruded forward between the optic nerves and elevated the A1 segments of the anterior cerebral arteries (Fig. 2). Twenty-three patients (46%) had retrochiasmatic tumors. These protruded posteriorly, filling the third ventricle and pushing back upon the basilar artery and midbrain (Fig. 3). Two patients had sellar tumors that did not distort the optic nerves or surrounding vessels but did enlarge the sella turcica.

**Tumor-Related Hydrocephalus**

Hydrocephalus was present in 24 patients. Its presence was significantly related to the location of the tumor \( p = 0.005 \). Seventeen (74%) of 23 patients with a retrochiasmatic tumor had hydrocephalus, compared to only seven (28%) of 25 patients with a prechiasmatic tumor. The two patients with sellar tumors did not have hydrocephalus.

Twelve of the hydrocephalic patients had a shunt inserted before their tumor surgery; the shunt was inserted 10 to 24 days before surgery in eight children and between 2 months and 5 years before surgery in three others. One child had hydrocephalus diagnosed by air encephalography at 1 year of age, at which time...
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FIG. 3. Magnetic resonance image showing a large cystic retrochiasmatic craniopharyngioma filling the third ventricle and producing hydrocephalus. Note the differing intensities in two distinct cystic portions of the tumor.

a shunt was inserted; 5 years later a craniopharyngioma was diagnosed and initial surgery on the tumor was performed. One child with a craniopharyngioma had been treated with a shunt for hydrocephalus in another country; he developed a subdural empyema that required therapy before his craniopharyngioma could be dealt with.

Three patients had shunts inserted after tumor surgery. The shunts were placed for treatment of cerebrospinal fluid rhinorrhea in one and for treatment of hydrocephalus due to recurrent tumor in two.

Operative Management

The surgical approach to the tumor was usually via a right frontal craniotomy with removal of the pterion in cases of retrochiasmatic tumor. Among our 50 patients, 37 (74%) had a right frontal craniotomy, two (4%) had a left frontal craniotomy, nine (18%) had both a frontal and pterional craniotomy, and two (4%) had bifrontal craniotomies. Forty-five patients were considered by the surgeon to have had total excision of their tumor at the time of surgery and five had subtotal tumor excision.

In 18 patients, all with retrochiasmatic tumors, the lamina terminalis was opened to aid in resection of the tumor. The tuberculum sellae was drilled away in three patients with retrochiasmatic tumors to allow access to the tumor between the optic nerves.

Postoperative Complications

Nine children (18%) suffered seizures in the immediate postoperative period. These seizures were always an isolated postoperative event, and none of these patients has a continuing seizure problem. Two patients had intraoperative bleeding resulting from injury to the internal carotid artery; both were left with a hemiparesis, and in one (whose craniotomy had been performed on the left side) there was also dysphasia. One patient developed spasm of the internal carotid artery which, in combination with operative hypovolemia, led to cerebral infarction and a hemiparesis.

Two patients developed rhinorrhea; both had had the tuberculum sellae drilled away to improve access to a retrochiasmatic tumor. One of these children went on to develop bacterial meningitis, which responded to antibiotic therapy.

Results

Follow-Up Evaluation

Three children have been lost to follow-up study. One child died in the immediate postoperative period following massive atelectasis. This child had been treated in another country and was referred to The Hospital for Sick Children with an infected shunt and a subdural empyema. On admission, he was suffering from cachexia and septicemia. Following treatment of his subdural empyema and eradication of his infection, he underwent a craniotomy for his craniopharyngioma. The tumor was totally removed, but 12 hours after the operation he aspirated and died. Postmortem examination revealed no residual tumor. Two other patients died 9 years after initial surgery. Both had recurrent tumors that were treated with surgery and radiation therapy but continued to cause problems; endocrine difficulties also contributed to the death of one of these patients.

For the remaining 46 patients, the follow-up period ranged from 1 to 14 years (mean 4.86 years). Eighteen (39%) of these patients were followed for at least 5 years postoperatively.

Tumor Recurrence

As of January 1, 1991, 17 patients (34%) have experienced recurrence of their tumor. Six of these were completely asymptomatic and the recurrence was detected on routine neuroimaging. Eight patients had headaches, five suffered deterioration in their visual acuity, and one had an increase in his need for 1-desamine-8-D-arginine vasopressin (DDAVP).

Thirteen patients had tumor recurrence after what was believed to be a total excision, and four after a subtotal excision. Among the 13 patients with total excision, five had a normal postoperative CT scan, whereas in eight CT showed either calcium or some enhancing tissue, suggesting that some tumor might have been left behind.

Evidence of recurrence came to light between 2 and 84 months following surgery (mean 2.46 years). Twelve of the 17 recurrences became evident within 3 years of surgery. Recurrences were managed in a variety of ways. Six patients had partial removal of the recurrent tumor followed by a course of radiation therapy. One child was treated with radiation therapy alone. Ten children had surgery alone: in five the recurrent tumor
FIG. 4. Left: Enhanced computerized tomography scan of a patient with cystic prechiasmatic craniopharyngioma. Right: Magnetic resonance image of the same patient 3 years after "total" removal of tumor showing recurrent intrasellar tumor.

was totally removed, three had a subtotal excision, and two had a partial excision.

Eight (47%) of the 17 patients with tumor recurrence had a second recurrence of tumor. In four it was found on routine follow-up CT scans and the remaining four had symptoms at the time of recurrence. All eight had been treated with surgery alone for their first recurrence. Five of these secondary recurrences were treated with radiation therapy; however, in three patients the second recurrence was only within the sella, so a transsphe- 
noidal approach was used to remove the residual tumor (Fig. 4).

Postoperative Visual Function

Eighteen patients showed no change from their pre-operative visual field testing; 13 of them had normal fields. Nine children showed improvement in visual field, with eight developing normal fields. In 19 patients, 16 of whom had no field defect before surgery, the visual field had deteriorated.

Twenty-five patients showed no change in visual acuity; 14 had normal acuity. Seven patients showed improvement in their visual acuity with six attaining normal acuity. Fourteen patients suffered deterioration in acuity; of these, 12 had exhibited normal acuity before surgery.

Endocrine Function

Endocrine status was described for 46 children. All were using some form of hormone replacement: 43 were receiving DDAVP, 41 cortisone, 38 thyroid therapy, 14 sex hormone replacement, and nine growth hormone. Thirty-four children were taking a combination of thyroid, cortisone, and DDAVP. Eight children required at least two of these hormones and four required replacement of only one hormone (DDAVP in two, thyroid in one, and cortisone in one). All of our patients were attaining normal stature due either to a normal growth process or to growth hormone therapy.

Twenty-four (52.2%) of 46 children were obese at follow-up evaluation; 16 harbored retrochiasmatic tumors, seven prechiasmatic tumors, and one a sellar tumor. Seven of the 24 children were obese before surgery. Two other patients were obese before surgery; one developed normal body configuration and one had been lost to follow-up study. Thirteen of these 24 patients have had difficulty in controlling their appetite, so weight gain is a significant problem.

Intellectual and Emotional Function

Twenty-seven children had a formal psychometric assessment at the time of follow-up examination. Full-scale intelligence quotient (IQ) scores were distributed as follows: two above 120, six between 110 and 119, 12 between 90 and 109, six between 80 and 89, and one below 69. Testing in 24 of these 27 children was performed at least 6 months after initial surgery.

Twenty-eight children underwent postoperative evaluation of their memory status, and 16 (57%) had some impairment of memory. The deficits varied in both the severity and the aspect of memory function affected, whether immediate or delayed, verbal or nonverbal. Ten of the 28 patients who underwent memory testing had suffered from retrochiasmatic tumors and seven of these had impaired memory. Eight of the 17 patients with prechiasmatic tumors suffered memory impairment. One child with a sellar tumor exhibited impaired memory. Frontal-lobe function was tested in nine patients (all over the age of 8 years) by administration of the Wisconsin Card Sorting Test; three of these were impaired relative to age-appropriate norms.

Educational status could be assessed in 39 children. Twenty-four were attending regular school, although some needed special help because of visual or memory deficits. Two children were attending special schools because of significant learning problems and one child was in a school for gifted children. One 4-year-old child was too young to attend school, four patients had graduated from high school, and six patients were attending college or university. Five children had behavior disorders. They were emotionally labile and posed problems for their families. In only one of these patients was the disorder so severe that the child could not function in a school environment.

Discussion

Historical Perspective

Before the development of steroid therapy, the morbidity and mortality rates after surgical treatment of craniopharyngioma were prohibitive. By the early 1950's, with the advent of steroid therapy, Matson was able to remove craniopharyngiomas safely and totally;12,16 however, very few other surgeons were able to duplicate his results. Their failure to do so was a result of the commonly accepted view that there is no line of cleavage between tumor and adjacent brain and that forcible removal of the craniopharyngioma would se-
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verely damage the hypothalamus and optic apparatus. Radiation therapy was therefore widely advocated for the treatment of craniopharyngioma and this, in its various modes, continues to be advocated for management of this tumor. Over the past 15 years, however, an increasing number of reports have identified various complications of radiation therapy. Furthermore, since irradiation does not necessarily prevent growth of a craniopharyngioma, we continue to see recurrent craniopharyngiomas in patients treated with biopsy or cyst aspiration and radiation therapy.6,7

Techniques for investigating and treating a patient with a craniopharyngioma have changed radically in the past 15 years. Modern neuroimaging tools allow earlier diagnosis of these lesions and better assessment of what surgery has accomplished. In situations where tumor has been left behind, surgeons have been encouraged to reoperate on recurrent tumors when they are small and easily removed. The operating microscope has allowed visualization of important structures and performance of the delicate maneuvers necessary to separate the craniopharyngioma from the visual structures surrounding it. Surgical tools such as the ultrasonic aspirator, which can decompress solid craniopharyngiomas, and the laser, which can vaporize foci of tumor and even fragment pieces of calcium, have facilitated safe excision, rendering tumors formerly considered inoperable both safely accessible and totally removable. No longer are we satisfied with subtotal or partial removal of a craniopharyngioma. Large, solid, calcified tumors that were difficult to deal with can now be removed safely.

Morbidity and Mortality

At The Hospital for Sick Children, total excision of a craniopharyngioma whenever possible has been the goal of treatment. Reports on different series of craniopharyngioma patients from this hospital have been published previously. The present series represents children treated within the last 15 years by microsurgical techniques and with the help of hormone replacement and modern neuroimaging methods. In this series, the rate of total resection as judged by the surgeon was 90%. However, among the 45 patients who underwent surgery, what was considered to be total excision, there have been 13 recurrences. The surgery was carried out with acceptable mortality and morbidity rates. One patient who was moribund when referred to us died postoperatively, yielding a mortality rate of 2%. Serious morbidity occurred in three patients who suffered injury to their internal carotid artery. Hemorrhage occurred in two patients, leading to a hemiparesis in one and a hemiparesis and dysphasia in the other. Spasm occurred in one patient, causing a hemiparesis.

Endocrine deficiency was present in all patients after surgery. However, modern endocrinological management has allowed them to live well and keep their hypopituitarism under control.

Vision was normal in 20 of 46 children. The other 26 had some degree of impairment. In some the deficits were severe but none was blind. Some children required large-print books but all had enough vision to be able to lead independent lives and function in school.

Weight gain has been a problem. For the 24 obese children in this series and their parents, unhappiness with excess weight and difficulty in controlling appetite were major sources of dissatisfaction. Excess weight was the main concern voiced at follow-up examination and was a complaint more often than visual, intellectual, or endocrine problems. In a society where fitness and slim bodies are praised, obesity has led to problems with peers at school who teased the patients, with parents at home who attempted to impose a strict diet, and with the way these children pictured themselves.

Education is a main concern in dealing with a child, ultimately determining the child's role in society. In the 27 children for whom intelligence tests were conducted, 26 had a full-scale IQ at or above the limits of average intelligence. However, memory was impaired in 16 of the 28 children tested. Memory impairment in patients with tumors in the region of the third ventricle has been ascribed to compression of the fornix cerebri and to deficiencies of vasopressin. In a study of patients treated with irradiation, surgery, or a combination of these techniques, Cavazutti, et al., found memory deficits immediately after treatment along with impairments in frontal-lobe functioning, the latter associated particularly with surgical therapy. Neither of these findings was confirmed in the present study. Moderate to severe impairments of immediate memory for verbal material were seen in a minority of patients only, and two-thirds of the patients tested for frontal-lobe function showed normal results. Among our patients, memory impairment did not interfere with school progress if intelligence was adequate. Of the 16 children who had memory impairment, 14 were attending regular school and making satisfactory progress and two required placement in a special school. Only one child was not able to study because of severe behavioral problems.

Quality of Life

It is still too early to say how these children will manage the problems of the adult world, but six are currently attending college or university. In assessing quality of life, we divided the patients into three groups. In the group of patients we considered normal or nearly normal, the tumor did not recur or, if it did, could be adequately managed with surgery. These patients had good control of their endocrine deficiencies, were attending or had attended regular school where they made progress, and had no behavioral problems or eating disturbances. The mildly handicapped group was composed of children whose tumor had not recurred or, if it had, could be managed with surgery alone, who had good control of their endocrine deficiencies, and who were attending or had attended regular school and made progress there. Some of these children may have re-
quired placement in a special school because of intellectual or visual deficits or because they experienced difficulties with weight control or excessive appetite. The severely handicapped group included patients with unstable tumor recurrence and poorly controlled endocrine status. These patients were not attending school because of behavior problems, or had major psychological disturbances or deficits that severely interfered with everyday life. Twenty-eight of our subjects belonged to the normal or nearly normal group, 12 were mildly handicapped, and four were severely handicapped. Three patients have been lost to follow-up study and three have died (one following surgery and the other two 9 years after surgery).

Conclusions

Our experience indicates that over 60% of craniopharyngiomas in childhood can be totally resected with minimal significant morbidity and mortality. We believe that the morbidity and mortality rates of patients who undergo an attempt at total resection of a craniopharyngioma are reasonable at the present time. Increasing experience with resection of these tumors and the advanced technology available should reduce these rates yet further so that children with craniopharyngioma can look forward to functioning in a more normal fashion. Their chances of leading a fully normal life will be greatest when their tumors are diagnosed and treated early because of the availability of improved diagnostic facilities and techniques.

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References


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