Surgical management of exophytic chiasmatic-hypothalamic tumors of childhood

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Sixteen children underwent 18 operations for radical resection of chiasmatic-hypothalamic tumors. The clinical presentation correlated with age: infants under 1 year of age presented with macrocephaly, failure to thrive, and severe visual failure; children aged 1 to 5 years predominantly had precocious puberty with mild visual deficits; and older children (> 5 years old) had slowly progressive loss of vision. All three infants had biologically aggressive tumors in spite of low-grade histology, and died from progressive tumor growth. Eleven of the 13 children aged 1 year or over are alive and well, without clinical or radiographic evidence of disease progression, 4 months to 489 years following surgery. Six of these patients, with a follow-up period of 10 months to 489 years (mean 27 months), have had no adjuvant therapy following radical surgical resection. The authors conclude that: 1) radical surgical resection of chiasmatic-hypothalamic tumors can be performed with minimal morbidity; 2) radical resection may delay the time to disease progression in older children and postpone the need for irradiation; 3) resection of postirradiation recurrent tumors may provide neurological improvement and long-lasting clinical remission; and 4) chiasmatic-hypothalamic tumors of infancy are aggressive neoplasms that require multimodality therapy.

KEY WORDS - astrocytoma · glioma · hypothalamus · optic glioma · radiation therapy · children

The optimal treatment of chiasmatic-hypothalamic gliomas is unclear. These neoplasms are often diagnosed in the first 5 years of life, are several centimeters in size, and occupy an extensive portion of the deep midline structures. The natural history of these tumors is quite variable, some may behave similar to hamartomas with minimal or no growth for many years, while others may progress with insidious loss of vision, vegetative compromise, and death.2,3,5,9,12-15,21,22,27 This course is especially unfortunate since, pathologically, these tumors are most commonly low-grade astrocytomas, often with pilocytic features, that are “sisters” to benign cerebellar astrocytomas which are associated with prolonged or normal survival and minimal disability.

The standard therapy for chiasmatic-hypothalamic tumors is irradiation.2,4,5,11,31-34 Stabilization of disease with objective tumor shrinkage on computerized tomography (CT) scans is seen in the majority of irradiated patients; however, the long-term deleterious sequelae of irradiating a large suprasellar mass in young children may be functionally devastating.2,22,25,26,29 The observation that many of these gliomas present exophytically in the suprasellar region with displacement of normal anatomy and the known long-term palliation that has followed radical subtotal resection of other low-grade midline astrocytomas of the septal region,24 cerebrum,18 and spinal cord,8 encouraged us to explore the feasibility of performing radical subtotal resections of exophytic chiasmatic-hypothalamic tumors of childhood. The subsequent clinical response is reported here.

Summary of Cases

Patient Population

Between June, 1984, and October, 1988, 16 children with exophytic chiasmatic-hypothalamic tumors underwent 18 surgical procedures at the New York University Medical Center. The patients ranged in age from 2 months to 21 years. Three children were less than 1 year old, seven were 1 to 5 years old, and six were between 5 and 21 years. There were 10 males and six females. At presentation, four patients had clinical evidence of neurofibromatosis. Three (aged 8, 12, and 21 years) had undergone radiation therapy 3, 6, and 10 years previously, respectively. None of the children had received prior chemotherapy or exhibited other neoplasms. Two patients, aged 2 and 6 years at first admis-
TABLE 1
Summary of clinical presentation in 16 patients

<table>
<thead>
<tr>
<th>Signs &amp; Symptoms</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>decreased visual acuity</td>
<td>11</td>
</tr>
<tr>
<td>field cut</td>
<td>5</td>
</tr>
<tr>
<td>strabismus/nystagmus</td>
<td>4</td>
</tr>
<tr>
<td>hydrocephalus/elevated intracranial pressure</td>
<td>6</td>
</tr>
<tr>
<td>macrocephaly</td>
<td>4</td>
</tr>
<tr>
<td>precocious puberty</td>
<td>4</td>
</tr>
<tr>
<td>diencephalic syndrome</td>
<td>4</td>
</tr>
<tr>
<td>seizures</td>
<td>3</td>
</tr>
<tr>
<td>behavior disorder</td>
<td>2</td>
</tr>
</tbody>
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Clinical Presentation

The presenting symptoms and signs are summarized in Table 1. There were three distinct age-related patterns of clinical presentation.

Infants. All patients aged less than 1 year presented with macrocephaly, failure to thrive, and severe visual failure. Two of the infants had severe hydrocephalus with signs of incipient herniation requiring emergency cerebrospinal fluid (CSF) shunting during the 1st hospital day. Computerized tomography demonstrated massive tumors in all infants (Fig. 1).

Children Aged 1 to 5 Years. Precocious puberty was the most common problem that brought the children aged 1 to 5 years to medical attention (four of the seven children). One child presented with acute hydrocephalus that required emergency shunting. Five of the children had either diminished visual acuity or visual field deficits on formal examination; however, only one child came to medical attention as a result of deteriorating vision. One child presented with psychomotor seizures and one had a classic diencephalic syndrome of 6 months’ duration.

Children 5 to 21 Years. Four patients presented with complaints relating to vision. In this group, three had neurofibromatosis and had received prior empiric irradiation for localized chiasmatic tumors; all of these had progressive deterioration in visual acuity. Two patients presented with somnolence, psychomotor seizures, and a behavior disorder. One patient had a hypothalamic hamartoma that had been partially resected at another institution 1 year prior to admission.

Surgery

All patients underwent surgical exploration with the intent to perform a radical resection. The Cavitron ultrasonic surgical aspirator (CUSA) and microscope were utilized in all cases and were indispensable surgical adjuncts. Visual evoked potentials were monitored in 50% of the patients; however, they did not consistently correlate with intraoperative manipulations or with the results of postoperative visual examination. The extent of resection was confirmed by contrast-enhanced CT alone in the first two patients and by CT and magnetic resonance (MR) imaging in the remaining 14 patients. Both of the secondary resections for recurrent tumor were evaluated pre- and postoperatively by MR imaging.

Fourteen children underwent a pterional craniotomy and two infants had a transcallosal approach as the primary treatment. Eleven children had radical resections (60% to 95% of tumor removed). All of the infants had limited resections (< 25% in two and 50% in one). Two of the older children with neurofibromatosis had a limited resection because the tumors were primarily infiltrative without a significant exophytic component.

Two children had a second radical resection performed at the time of tumor recurrence. Both had undergone a pterional craniotomy with 80% tumor resection at their primary surgery and received postoperative irradiation. At recurrence, these tumors had grown exophytically into the third ventricle, necessitating a transcallosal resection. Both had a less than 90% resection at the second operation.

Operative Results

Pathology. Twelve children had low-grade astrocytomas, two with pilocytic features. One infant had a grade III/IV astrocytoma and died 4½ years after resection. There was one ganglioglioma and one hypothalamic hamartoma; one patient with neurofibromatosis, who had received irradiation, underwent a nondiagnostic biopsy. There was no correlation between pathol-
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**Fig. 2.** Radical (> 90%) resection in Case 1. a: Preoperative magnetic resonance image. b: Operative photograph showing the left carotid artery (small arrow) and optic nerve (double arrow) displaced by a tumor (large arrow). c: Operative photograph after resection. d: Magnetic resonance image 3 years after surgery.

**Outcome.** There was no operative mortality. All three infants died of progressive tumor growth 13, 24, and 54 months after surgery. The infant who survived 54 months was severely disabled for the entire period. The families of all of the infants had refused any postoperative adjuvant therapy.

The child with radical resection of a hypothalamic hamartoma did not demonstrate increased tumor on radiological studies but continued to experience clinical deterioration as a result of his seizure disorder and preoperative hypothalamic dysfunction. He died 3 years following surgery. One child had progressive tumor growth and failure of vision 2 months following radical (70%) tumor resection. He is alive with stable disease 20 months after initiation of chemotherapy (vincristine and actinomycin D).

Eleven patients are alive and well 4 months to 4 1/2 years following surgery. Nine of these patients had a radical resection and two were the older children with neurofibromatosis who had received prior irradiation. Of the nine patients who underwent radical resection, six have had no further therapy during a follow-up period of 10 months to 4 1/2 years (mean 27 months). All are clinically stable with normal developmental milestones and/or school performance and MR imaging has revealed no evidence of tumor progression. The child with the diencephalic syndrome had complete recovery with normal weight, growth, and development within 3 months of surgery (80% resection). The oldest patient who had received irradiation 10 years prior to surgery had a 90% resection of a predominantly cystic tumor. She is clinically improved, with MR imaging evidence of a stable condition 12 months postsurgery.

Neither of the two children who underwent a second radical resection has received further therapy. Both remain clinically and radiographically stable 8 and 10 months postoperatively.

No child suffered a deterioration of vision or onset of diabetes insipidus as a result of surgery. Two-thirds of the patients experienced a transient syndrome of inappropriate antidiuretic hormone release (SIADH). This resulted in metabolic seizures in three patients secondary to hyponatremia. There were no permanent neurological sequelae or seizure disorders as a result of the SIADH.

**Illustrative Cases**

**Case 1: Radical Resection**

This 15-year-old boy presented with a right homonymous hemianopsia. Neurodiagnostic imaging demonstrated a tumor arising exophytically from the chiasmatic-hypothalamic region on the left (Fig. 2a). The tumor was exposed through a left pterional craniotomy. A gross nearly total resection was obtained (Fig. 2b and...
c) with a minimal amount of tumor left en plaque on the inferior surface of the chiasm. A single perforating vessel of the A\textsubscript{1} anterior cerebral artery segment was sacrificed during the operation, resulting in a postoperative frontal infarction with transient hemiparesis and expressive dysphasia. The patient is alive and well without recurrent tumor 36 months following surgery (Fig. 2d).

Case 2: Subtotal Resection

This 2½-year-old boy presented with precocious puberty and diminished visual acuity. Magnetic resonance imaging demonstrated an exophytic suprasellar chiasma-hypothalamic tumor (Fig. 3 left). The tumor was exposed through a right pterional craniotomy (Fig. 4). The optic nerves were normal in size but the chiasm and optic tract were markedly stretched and elevated by the exophytic mass. A subtotal (60%) resection of the tumor was accomplished with decompression of both optic nerves and chiasm. Following surgery, the patient's vision improved and he has remained clinically stable for 24 months. No growth of the residual tumor was found on MR imaging 2 years postoperatively (Fig. 3 right).

Case 3: Cyst Fenestration and Tumor Resection

This 21-year-old woman with neurofibromatosis received irradiation for a suprasellar tumor at the age of 10 years. At her current admission, she presented with progressive deterioration of visual acuity. On MR imaging, a cystic suprasellar tumor was found compressing the left optic tract and chiasm (Fig. 5 left). The tumor was approached through a left pterional craniotomy. At surgery, the cyst was fenestrated and a small nodule of tumor was resected. Postoperatively, the patient's vision improved and she has remained clinically and radiologically stable for 12 months. An MR image obtained following surgery demonstrated collapse of the tumor-associated cyst and no residual tumor enhancement (Fig. 5 right).

Discussion

Tumor Classification

Gliomas of the optic pathway comprise a broad spectrum of tumors ranging from tubular thickening of the optic nerves and chiasm to massive exophytic lesions that exhibit variable biological behavior. This tremendous diversity has made it extremely difficult to understand the natural history and analyze the response to treatment. Several different classification schemas have been suggested using anatomical, clinical, functional, and pathological categories.

Fletcher, et al.\textsuperscript{9} suggested a clinicanoanatomical classification based on CT scanning: 1) tubular thickening of the optic nerves and chiasm; 2) suprasellar tumor with contiguous optic-nerve expansion; 3) suprasellar tumor with contiguous optic-tract extension; and 4) globular chiasmatic tumors. The value of their classification system is the recognition that the CT appearance of the first three categories is pathognomonic of an optic-pathway tumor, obviating the need for diagnostic
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Fig. 5. Magnetic resonance (MR) images in Case 3, with fenestration of cyst and resection of tumor postirradiation. Left: Preoperative MR image showing a left suprasellar cyst. The sylvian fissure cysts (arrows) are porencephalic secondary to a perinatal infarct. Right: Postoperative MR image.

biopsy. The globular lesions cannot be accurately delineated from other suprasellar tumors and require histological confirmation. The utility of this classification for prognosis and treatment planning is uncertain.

McCullough and Epstein have suggested a system based on anatomical staging and visual function utilizing standard oncological staging terminology (that is, the "T" stage). They classified the location of the tumor by its most posterior extension, so that T1 denotes a unilateral optic nerve, T2 bilateral optic nerves, T3 the optic chiasm, and T4 the hypothalamus/thalamus. Visual function was graded V0 to V4: from normal vision to complete blindness in both eyes. This classification addresses the apparent increase in morbidity and mortality observed in more posteriorly located tumors.

Sugita and Kageyama have proposed a clinicopathological grouping by age into types of tumor affecting infants and children. The infant type of tumor is large and invades the hypothalamus early in the disease. These lesions present with severe loss of vision, intracranial hypertension, and hypothalamic dysfunction, and they carry a poor prognosis. In contrast, the type seen in children is localized to the optic nerve, chiasm, and tract with minimal growth; this type has a good long-term prognosis.

Radiation Therapy

Radiation therapy has been the primary mode of treatment advocated for progressive disease. Stabilization of tumor size or diminished tumor volume following irradiation has been well documented; however, clinical improvement in visual function and neurological deficits occur in only a minority of cases. Unfortunately, the failure rate and deleterious sequelae of irradiation are significant. Progressive disease may occur in over 50% of patients following radiotherapy. Fletcher, et al., have described progressive cerebral calcification and remote infarction as long-term risks of irradiation. Packer, et al., and Duffner, et al., noted a high incidence of severe intellectual impairment in the first few years of life in children who were irradiated. Delayed large-vessel occlusion, moyamoya disease, and late cerebral infarction have been reported in children receiving 3000 to 6000 rad for chiasmatic tumors.

Chemotherapy

Chemotherapy has been advocated as an alternative to irradiation for young children with chiasmatic-hypothalamic tumors. Packer, et al., treated 24 children, most of whom were under 3 years of age, with combination chemotherapy (vincristine and actinomycin D). Fifteen of the children had no evidence of tumor progression and all were alive after a median follow-up period of 4.3 years. The goal of the protocol was to postpone irradiation, allowing brain maturation, rather than to obviate the ultimate need for radiotherapy.

Clinical Course

On CT and MR imaging, the patients in this series all presented with bulky exophytic chiasmatic-hypothalamic tumors that would be classified as T4 by McCullough and Epstein. In the majority of these children, the extensive mass of these lesions precluded preoperative delineation of involvement of contiguous structures. At surgery, half of the tumors had contiguous optic-nerve involvement while the other half were multilobular globular tumors. In our patients there was no consistent relationship between, on one hand, preoperative visual function (V stage), presence of diencephalic syndrome, extent of resection, or duration of event-free survival and the cliniconeuatomic classifications of Fletcher, et al., or Duffner, et al.

In agreement with the effect of age on the prognosis reported by Sugita and Kageyama and Kanamori, et al., the three infants in our series all had a malignant course in spite of benign histology. In a more recent series, Kageyama, et al., also noted rapid tumor growth, an aggressive clinical course, and poor outcome in the three infants in their series of 10 children with chiasmatic tumors. However, since all of our patients had large chiasmatic-hypothalamic tumors, we take issue with these authors’ contention that this type of tumor occurs primarily in infants and carries an inevitably poor prognosis. We believe that the poor outcome in infants is a result of the relationship between age and tumor biology rather than of tumor size or location.

Surgical Management

Previously, radical surgical resection of chiasmatic-hypothalamic tumors was reserved for symptomatic hamartomas with significant reported morbidity and mortality rates. The role of surgery in astrocytic tumors was limited to biopsy, with irradiation considered to be the definitive mode of treatment. In contrast, Gillett and Symon have commented on the relative
simplicity of surgical resection of chiasmatic-hypothalamic gliomas. They noted that most of their patients had visual symptoms secondary to compression of the optic chiasm and tracts by the exophytic component of the tumor. None of their seven adult patients had significant deterioration in neurological or visual function after radical resection. Albright and Sclobassi reported two children who had radical resections of chiasmatic gliomas without any morbidity. They recommended the use of the CUSA and intraoperative visual evoked potentials as surgical adjuncts. One of their patients, an infant, received no further therapy and has remained clinically and radiologically stable for 1 year.

Our children have tolerated surgical resection with minimal morbidity and no mortality. The one patient with significant permanent sequelae of surgery was the 15-year-old boy described above (Case 1) who suffered a postoperative infarction and mild residual dysphasia. We believe this was due to a technical error that can be avoided in the future. Ten of our 16 patients have no evidence of tumor progression or recurrence following surgical resection without any subsequent adjuvant therapy. Although the follow-up period is short, it appears likely that surgery alone may be equal or even superior to chemotherapy in delaying the time to tumor progression and need for irradiation. In addition, there is the possibility that some of these tumors may remain in remission indefinitely.

Surgical intervention appears to be useful in selected recurrent tumors. The children with neurofibromatosis were all benefited clinically and radiographically following resection of tumors that had progressed several years after primary irradiation. Drainage of a radiation-induced tumor cyst and resection of solid tumor were accomplished in one patient (Case 3) without any additional technical difficulties.

The high failure rate among the infants in our series may reflect inadequate surgical resection, since they were treated early in our experience. It is conceivable that, with more radical surgery and possibly chemotherapy, the prognosis may be improved.

Conclusions

1. Radical resection of chiasmatic-hypothalamic tumors may be performed with minimal morbidity and mortality.
2. Radical resection may delay the time to disease progression in older children and postpone the need for irradiation or chemotherapy.
3. Partial resection of recurrent tumors postirradiation may offer significant clinical improvement and remission.
4. Chiasmatic-hypothalamic tumors of infancy are aggressive neoplasms that may require multimodality therapy.

References

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