The long-term outcome after surgical treatment of dorsally exophytic brain-stem gliomas

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Dorsally exophytic brain-stem gliomas represent a distinctive subgroup of pediatric brain-stem neoplasms that are amenable to radical excision because of their benign histology and growth characteristics. However, their attachment to the floor of the fourth ventricle invariably precludes complete tumor excision. The long-term behavior of the residual tumor remains a subject of concern. To address this issue, the authors reviewed their experience with 18 dorsally exophytic brain-stem gliomas treated between 1974 and 1990. At operation, the tumors filled the fourth ventricle, fungating out of a broad-based area of the dorsal brain stem. The exophytic tumor was resected, but no attempt was made to remove tumor from the brain stem. Histological examination showed that 16 of the tumors were grade I or II astrocytomas, one was a ganglioglioma, and one was an otherwise benign-appearing glioma with several foci of anaplasia that was classified as a grade III astrocytoma. The latter patient was one of only two in the series to receive postoperative radiation therapy; both cases so treated have no evidence of disease on follow-up imaging studies 61 and 135 months postoperatively. One other child who had stable disease postoperatively died of shunt malfunction 18 months after tumor excision. Serial radiographic studies in the other 15 patients have shown no evidence of disease in three, stable residual disease in eight, and tumor enlargement 12, 28, 40, and 84 months postoperatively in four (median follow-up period 113 months). Each of the four patients with tumor regrowth underwent repeat tumor excision. Two of these children received perioperative radiation therapy at the time of disease progression and both showed reduction in tumor volume 28 and 65 months after their second operation. In contrast, both patients who did not receive radiotherapy at the time of disease progression had further tumor enlargement 48 and 84 months after their second operation and underwent a third tumor resection, one received postoperative radiation therapy and has no evidence of disease 58 months after his third operation and the other child has stable disease 27 months postoperatively. Histological examination of tumor specimens obtained at second and third operations showed no change from the appearance of the tumor on the initial resection. The authors conclude that the majority of dorsally exophytic brain-stem gliomas can be managed successfully with subtotal excision and, if necessary, cerebrospinal fluid diversion. The small percentage of tumors in this series that showed recurrent growth remained benign histologically. In these patients, repeat tumor resection and radiotherapy appeared to be effective in maintaining long-term disease control.

KEY WORDS • astrocytoma • brain-stem tumor • fourth ventricle • radiation therapy • children

Brain-stem gliomas account for 10% to 20% of all pediatric brain tumors and 20% to 25% of all infratentorial tumors. The majority of these neoplasms are biologically malignant intrinsic tumors that infiltrate extensively into the surrounding brain stem. Because of the malignant behavior and infiltrative growth characteristics of these lesions, surgical intervention is rarely of benefit and is potentially hazardous. Treatment of these lesions has therefore relied predominantly on nonsurgical modalities. With conventional fractionated radiotherapy, temporary disease control is achieved in a large percentage of patients. Unfortunately, these tumors typically recur and often lead to inexorable neurological deterioration and death within 2 years of diagnosis. At best, 5-year survival is obtained in about 30% of patients. Accordingly, recent work at a number of centers has been directed at optimizing radiotherapeutic and, in some cases, chemotherapeutic strategies in the hope of ameliorating the grim outlook for patients with these tumors.

Although surgery assumes a limited role in the management of diffusely infiltrating intrinsic brain-stem gliomas, it has become apparent in recent years that outcome in several subgroups of focal brain-stem tumors may be substantially improved by aggressive surgical intervention. Epstein, et al. have demonstrated that gliomas involving the cervicomedullary junction...
are generally benign and predominantly displace rather than invade normal structures. With aggressive surgical excision, patients harboring these lesions may enjoy prolonged survival.²⁷,⁴⁶ Encouraging results have also been reported with radical debulking of focal low-grade gliomas that arise more rostrally within the brain stem²⁵,²⁶ and with aspiration or subtotal excision of cystic low-grade gliomas.⁹,¹⁵,¹⁶ Hoffman, et al.¹⁶,²⁴,²⁶ have previously identified an additional subgroup of brain-stem gliomas that grow exophytically from the floor of the fourth ventricle and are also characterized by a favorable short-term response to surgical treatment.

Although radical debulking of focal or dorsally exophytic brain-stem gliomas can generally be achieved safely with appropriate microsurgical techniques, complete tumor excision is not feasible since these lesions originate from within the brain stem and blend imperceptibly into the surrounding normal structures without a distinct tumor-brain stem interface.⁹,²⁵ Accordingly, a substantial component of tumor is often left at surgery. A major unresolved issue in the management of these lesions concerns the role of radiation therapy for the treatment of this residual tumor.

Since 1974, it has been our practice in patients with dorsally exophytic brain-stem gliomas to reserve radiation therapy for those with evidence of progressive disease. However, the fate of the residual tumor has always been a subject of some concern. It has previously been uncertain how frequently these lesions manifest recurrent growth and, more importantly, whether they ultimately demonstrate a potential for malignant progression. To address this issue, we reviewed our long-term results in patients with dorsally exophytic brain-stem gliomas managed since 1974.

Clinical Material and Methods

Case Material

Between 1974 and 1990, 18 patients (10 girls and eight boys) with dorsally exophytic brain-stem gliomas were treated at The Hospital for Sick Children. Such tumors accounted for approximately 19% of all brain-stem gliomas treated at our institution during this period. The patients ranged in age from 1 month to 13 years at the onset of symptoms and from 1 to 14 years at the time of diagnosis. Initial symptoms developed before 1 year of age in five children, all of whom manifested failure to thrive as a result of chronic vomiting. The diagnosis in these infants was invariably delayed; all but one was symptomatic for more than 1 year before diagnosis. These patients typically underwent exhaustive medical evaluation before the brain-stem tumor was detected. The older patients presented with a combination of headache, vomiting, and ataxia. Because symptoms were often insidiously progressive, many of these older children were also symptomatic for an extended period before diagnosis.

Examination revealed papilledema in 13 children, ataxia in 12, torticollis in six, prominent nystagmus in six, and cranial nerve dysfunction in seven. None of the children had significant long-tract signs.

Imaging Studies

Seventeen of the 18 patients underwent preoperative computerized tomography (CT) studies. Magnetic resonance (MR) imaging was also performed in recent years. In the one patient treated in 1974, the lesion was identified by ventriculography and angiography.

On CT, the tumor characteristically appeared hypodense or isodense in relation to the surrounding brain, and enhanced brightly after the intravenous administration of contrast medium. Small cystic components were seen in several lesions. The fourth ventricle was often largely obliterated by tumor, although on sagittal CT reconstruction or MR imaging, a cap of cerebrospinal fluid (CSF) was sometimes detectable dorsally or at the rostral and caudal poles of the tumor. Ventrally, tumor blended imperceptibly into the brain-stem surface. Varying degrees of obstructive hydrocephalus were present in 15 children.

Initial Operative Treatment

Five children with profound obstructive hydrocephalus and severe symptoms of increased intracranial pressure underwent placement of a ventriculoperitoneal (VP) shunt as a stabilizing measure in preparation for tumor resection. One other child had received a VP shunt for a presumed diagnosis of “aqueductal stenosis” 2 years before the posterior fossa tumor was detected radiographically.

All 18 patients underwent posterior fossa exploration with a midline suboccipital approach; the posterior arch of Cl was often removed to enhance exposure of the inferior pole of the tumor. The exophytic component of the tumor typically splayed apart the cerebellar tonsils and, with careful dissection, was separable from the surrounding cerebellar tissue. Aggressive debulking of the exophytic tumor was facilitated by the use of an ultrasonic aspirator. A broad area of attachment to the floor of the fourth ventricle was invariably encountered at the base of the tumor. Despite the use of microsurgical techniques, no definite tumor-brain stem interface was detectable. No attempt was made to resect tumor from within the brain stem. Accordingly, none of these patients had total tumor resection. In eight patients, a ventriculocisternist catheter that extended from the third ventricle through the aqueduct and fourth ventricle into the cisterna magna was placed at the completion of tumor resection.

Tumor Histology

Sixteen tumors were classified as grade I or II astrocytomas. One other tumor had several small foci of mitoses and necrosis in an otherwise low-grade lesion and was classified as a grade III glioma. Another tumor showed a small cluster of pleomorphic neurons amid a typical low-grade glioma and was classified as a ganglioglioma.

Radiation Therapy

Postoperative radiotherapy was administered to only two patients in this series: the child with a grade III astrocytoma and a child with a low-grade glioma that showed particularly widespread infiltration of the brain-
children: normal children: were obtained from stem surface. Both patients received a total dose of 5250 cGy in 175-cGy fractions from a 6-MV linear accelerator to a generous volume of the posterior fossa and midbrain.

Postoperative Follow-Up Evaluation

All patients but one (who was referred for surgery from a foreign country) had serial clinical examinations performed at our institution 3, 6, and 12 months postoperatively. Follow-up CT and/or MR studies were obtained at or before the scheduled clinic visit except for the child who underwent surgery in 1974; her first CT scan was obtained 1 year postoperatively. Subsequent clinical and radiographic follow-up evaluations were performed on a yearly basis, provided that the patient remained free of symptoms; the development of recurrent symptoms led to a prompt re-evaluation. Patients who had no evidence of tumor regrowth for at least 10 years were then followed biennially.

Results

Postoperative Morbidity

There were no perioperative deaths in this series, and neurological morbidity was generally limited to transient exacerbation of preoperative ataxia, dysmetria, nystagmus, and cranial nerve deficits (particularly sixth and seventh nerve paresis). One child developed a new hemiparesis postoperatively. Cranial nerve dysfunction typically resolved completely within 1 year of surgery. Persistent cranial nerve deficits were present in five children: four had a sixth nerve paresis, two had a seventh nerve paresis, and one had ninth and 10th nerve dysfunction. Ataxia, dysmetria, and nystagmus generally improved substantially over time, and all children were ultimately able to resume a full range of normal activities. Other postoperative morbidity included aseptic meningitis, CSF leakage through the wound with subsequent bacterial meningitis and shunt infection, and C1–2 subluxation in one patient each.

Although an open communication between the aqueduct of Sylvius, the fourth ventricle, and the foramina of Magendie and Luschka was invariably re-established by the conclusion of the tumor debulking, six patients with preoperative hydrocephalus who did not receive VP shunts required shunt placement within 2 months after surgery because of progressive ventricular dilatation. It is of interest that five of these six patients had received internal transaqueductal catheters at the time of their initial operation.

Outcome After Initial Treatment

Seventeen patients were alive at the conclusion of the study, with follow-up periods ranging from 33 to 212 months (mean 110 months, median 113 months). One child who had stable disease postoperatively died of a shunt malfunction at another hospital 18 months after tumor excision. The two patients who received postoperative radiotherapy have no evidence of residual disease on follow-up imaging 61 and 135 months after surgery. Both children suffered radiation-induced alopecia and one developed isolated growth hormone deficiency with resultant short stature.

Serial clinical and radiographic evaluations in the 15 other patients who were followed to the conclusion of the study have shown the complete disappearance of residual tumor in three children, stable residual disease in six (Fig. 1), and obvious tumor regrowth in four (Fig. 2). In the latter four patients, tumor enlargement was detected radiographically at 12, 28, 40, and 84 months after surgery, and was associated with recurrent symptoms in all but the third patient in whom a large recurrence was detected solely by CT. In three patients, the recurrent tumor contained a large cystic component (Fig. 2B, C, and D).
Tumor Diminished

Management of Progressive Disease and Outcome

Three patients underwent a second exploration for tumor excision when tumor regrowth was detected. The fourth child received radiotherapy at the time of disease progression; although the solid component of the tumor diminished slightly in size on serial imaging studies, the patient became increasingly symptomatic from progressive enlargement of a multiloculated cystic component of the tumor and ultimately underwent repeat exploration. In each of the four patients, the exophytic solid tumor component was relatively well circumscribed from the surrounding structures and was radically resected. In the three cystic tumors, the exophytic portion of the cyst wall was excised, leaving intact the attachment of the cyst to the brain stem. As in the initial operations, no attempt was made to resect tumor growing within or directly upon the brain stem. One patient received postoperative radiotherapy.

Both patients who received radiotherapy pre- or postoperatively at the time of tumor enlargement have shown a progressive decrease in tumor volume 28 and 65 months after their second operation (71 and 111 months, respectively, after initial surgery). The other two patients exhibited further tumor regrowth 48 and 84 months after their second operation and underwent a third tumor resection. One of these two patients received postoperative radiotherapy and has no evidence of residual disease 58 months after the third operation (165 months after initial surgery). The other child has stable disease 27 months postoperatively (159 months after initial surgery) (Fig. 2E and F). One of the three children who received radiotherapy for disease progression has subsequently manifested short stature as a result of growth hormone deficiency. No other radiation-related neuroendocrine deficits have been detected.

Histology in Patients With Tumor Progression

Histological examination of the tumor specimens from the second and third operations in each of the four patients with tumor regrowth showed no significant change from the appearance of the tumor obtained at the initial exploration other than a more striking prominence of Rosenthal fibers. In addition, vascular hyalinization was noted in the specimen obtained from the patient who underwent radiotherapy before her second tumor excision. No trend toward increased anaplasia was detected in any of the tumor specimens obtained at re-exploration.

Discussion

It has become apparent during the last decade that the prognosis for patients with brain-stem gliomas is critically dependent on the location and growth characteristics of the tumor. In contrast to the dismal outlook that typically characterizes diffuse biologically malignant intrinsic gliomas, focal lesions of the cervicomедullary junction[14,23] or midbrain[12,22] and dorsally exophytic tumors arising from the fourth ventricular floor[3,14,16,19] are generally benign histologically and
Dorsally exophytic brain-stem gliomas

amenable to radical subtotal excision. With aggressive surgical therapy, patients harboring these benign lesions may enjoy prolonged survival. However, the attachment of these tumors to critical brain-stem structures almost invariably precludes complete excision. This raises important issues regarding the long-term behavior of the residual tumor and the role of postoperative radiotherapy in the management of these lesions. In view of the risks to the developing nervous system of radiotherapy and its deleterious long-term effects on neuroendocrine function, it would be desirable to defer employing this modality for as long as possible provided that such an approach is not associated with an unacceptable incidence of disease progression. Since 1974, we have followed this strategy in the management of virtually all dorsally exophytic brain-stem gliomas based on our preliminary observations that, at short-term follow-up evaluation, such lesions generally showed a low incidence of disease progression.

The long-term results reported here support the efficacy of this approach. Only four of 16 patients in this series, who did not receive radiotherapy after their initial operation, showed evidence of tumor progression. Those tumors that did demonstrate recurrent growth remained benign histologically and were amenable to a second attempt at radical tumor excision.

Since the number of children with recurrent disease was small, and the management of such patients was individualized, it is not possible to make any strong statements regarding the optimum therapy for patients with tumor progression. Radiotherapy proved to be effective in preventing further tumor growth in the two patients who were treated with this modality at the time of disease progression (as well as in the two who received radiotherapy initially). In contrast, the two patients who underwent re-exploration but did not receive radiotherapy showed subsequent tumor growth; in both cases this occurred several years after the initial recurrence and was amenable to a third tumor resection. The decision to withhold radiotherapy after an initial recurrence must therefore take into account a number of factors such as age and growth of the patient.

We conclude that the majority of dorsally exophytic brain-stem gliomas can be managed successfully with subtotal excision and, if necessary, CSF diversion. In this series, the small percentage of tumors that showed recurrent growth remained benign histologically and were amenable to repeat tumor excision.

References


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