Intrinsic brain-stem tumors of childhood: surgical indications

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This report summarizes the first author's experience with radical excision of intrinsic non-exophytic brain-stem gliomas in 34 pediatric patients. On retrospective analysis, these tumors may be classified into three subgroups: focal, diffuse, and cervicomedullary. A focal neoplasm is a circumscribed mass less than 2 cm in diameter and without associated edema. Tumors of a larger size or in which the "focal" neoplasm is associated with a large area of apparent edema are classified as diffuse. Cervicomedullary neoplasms occur at the junction of the medulla and spinal cord and involve both of the structures but do not extend rostrally into the pons.

A radical tumor excision was carried out in all patients, and the only mortality and morbidity occurred in children harboring diffuse gliomas. All of the diffuse gliomas were malignant (grade III or IV astrocytomas), whereas three of the four focal astrocytomas and all of the cervicomedullary tumors were grade II astrocytomas. No patient with a diffuse astrocytoma was benefitted by surgery, while two of the focal astrocytomas and all of the cervicomedullary neoplasms either became stable or improved postoperatively. It is concluded that, although primary radical excision is recommended for cervicomedullary neoplasms, which are often benign, the more traditional radiation therapy and/or chemotherapy remain appropriate for tumors above the medulla.

KEY WORDS • brain stem • glioma • astrocytoma • pediatric surgery • glioblastoma

Intrinsic brain-stem tumors have traditionally been treated with irradiation and adjunctive chemotherapy, with relatively little success. The neurological course may be transiently improved, but then it invariably progresses after a relatively short remission, and children rarely survive more than 1 or 2 years after the primary diagnosis. Although some neurosurgeons have recommended a brain-stem biopsy to confirm the presence and pathological grade of the neoplasm, only a few have suggested that it might be technically feasible to carry out a radical tumor excision and induce clinical remission (and perhaps in rare circumstances effect a cure). Despite this generally dismal prognosis, it has been our perspective that there might be at least a few brain-stem gliomas that were both low-grade and surgically resectable. On this basis, it was elected to study a group of afflicted children, using their detailed clinical and neurodiagnostic examinations in conjunction with operative findings to ascertain whether it was possible to predict preoperatively which patients might benefit from surgery. This report summarizes the first author's experience with radical excision of intrinsic non-exophytic brain-stem gliomas in 34 patients.

Summary of Cases

Tumor Location

Retrospective analysis has suggested that the most important factors for assessing the potential benefit of surgery are the size and location of the tumor within the brain stem, the presence or absence of associated edema, and the clinical symptomatology. For purposes of surgical classification we have identified three tumor subgroups: focal, diffuse, and cervicomedullary. A focal neoplasm is a circumscribed mass less than 2 cm in diameter without associated edema. A diffuse tumor has a large hypodense component with or without a "focal" component. Cervicomedullary neoplasms involve the lower two-thirds of the medulla and the rostral segments of the spinal cord. In this series of 34 patients, 22 neoplasms were diffuse, four focal, and eight cervi-
comedullary. The latest neurodiagnostic imaging is essential to identify these subgroups. It has become apparent that magnetic resonance imaging (MRI) is an indispensable adjunct in the assessment of brain-stem neoplasms. This is particularly important with cervicomedullary tumors, where the sagittal view defines the rostral and caudal limits of the tumor (see Fig. 2 right).

Clinical Presentation

All 22 patients with diffuse neoplasms had the early signs and symptoms typical of a brain-stem glioma. These included multiple and often bilateral cranial nerve dysfunction associated with spasticity in the lower extremities. The clinical course was rapidly progressive and, despite radiation therapy, all of these patients were severely disabled at the time of surgery.

Three of the four patients with a focal tumor had an atypical clinical presentation, with dysfunction in only one cranial nerve and little or no spasticity in the lower extremities. The clinical course in these three patients was insidious, and after radiation treatment they had remission lasting from 12 to 24 months. Following this, significant neurological deterioration gradually evolved and two of these patients were severely disabled at the time of surgery. The fourth patient with a focal tumor had the classical symptoms of a brain-stem glioma.

The eight patients with cervicomedullary tumors had lower cranial nerve dysfunction associated with hemiparesis, quadriparesis, and spasticity. The clinical course was consistently protracted, and significant disability did not occur until 1 to 3 years following radiation therapy.

Operative Technique

All patients were primarily treated with irradiation and chemotherapy. They were referred for surgical assessment when there were clinical signs of tumor progression, and they were all moderately or severely disabled at the time of surgery. Forty-eight hours prior to surgery, patients were started on a large dose of corticosteroids (Solu-Medrol: methylprednisolone sodium succinate, 10 mg/kg; or Decadron: methylprednisolone sodium phosphate, 1.5 mg/kg in 24 hours).

In all cases an incision was made over the portion of the tumor that was closest to the surface of the brain stem. In 20 patients the incision was made through the floor of the fourth ventricle (Fig. 1), and in six patients tumors in the antero-lateral portion of the pons were exposed through a retromastoid approach. In the eight patients with cervicomedullary neoplasms the rostral region of the spinal cord and the lower medulla were exposed and a myelotomy in the midline of the spinal cord was extended rostrally into the medulla (Fig. 2). Tumors approached through the floor of the fourth ventricle were exposed by superior retraction of the cerebellar tonsils and vermis. In a few cases it was necessary to incise the inferior vermis (not more than 1.5 cm) to visualize adequately the more rostral region of the fourth ventricle.

Fig. 1. Computerized tomography scan showing a “diffuse” pontine glioma. Despite the focal appearance of the enhancing component of the neoplasm the associated edema is indicative of a grade III or IV astrocytoma.

Inspection of the ventricular floor invariably disclosed that the median raphe was displaced away from the tumor. In addition, there was always a focal bulging of the ependymal lining in the area where the tumor was closest to the surface of the ventricle. In 10 patients, the ependyma was disrupted by the underlying neoplasm and the tumor was immediately obvious on the floor of the ventricle.

In the first 15 patients in this series the tumor was removed with the Cavitron ultrasonic aspirator (CUSA),* and in the last 19 patients the entire procedure was carried out with the laser. Although ultrasonic dissection was technically satisfactory, visibility was limited by the restricted exposure and the relatively large CUSA handpiece. The laser was most effective in the 4-to 6-W power range. The neoplasm was visualized and pathological specimens were secured, after which the tumors were vaporized fragment by fragment. The resultant laser char made it necessary to interrupt the dissection many times to gently remove the thin layer of blackened tissue and adequately visualize the residual neoplasm. In all cases it was intended that dissection remain within the tumor tissue, so no effort was made to identify normal white matter around the area from which the tumor was removed. It must be emphasized

* Cavitron ultrasonic aspirator manufactured by Cavitron, Cooper Medical, 88 Hamilton Avenue, Stamford, Connecticut.
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that the surgical goal was to obtain a radical tumor excision, but it was assumed that gross total excision was probably not obtainable in the overwhelming number of cases.

Radical excision was technically more feasible when the tumor was approached through the floor of the fourth ventricle than via the retromastoid approach. Although the retromastoid approach provides excellent exposure of a bulging pons, excision of the tumor must be carried out between the fifth and seventh cranial nerves and visibility is somewhat restricted.

Brain-stem evoked potentials were monitored in the last 10 patients.† This provides a useful continuum of electrical data, but it is too early in our experience to suggest that this is a mandatory part of the procedure.

Postoperative Course

The immediate postoperative course was related to the preoperative neurological status. Patients who were severely disabled prior to surgery recovered very slowly, whereas those who were less impaired improved more rapidly. The most common complication was unilateral sixth and seventh nerve paralysis. This occurred in four patients, was clearly related to injury to the facial colliculus in the floor of the fourth ventricle, and was invariably permanent. Four patients had serious difficulty with swallowing. Two of these developed aspiration pneumonia, and one died of this complication.

Operative Results

**Diffuse Tumor.** All 22 patients with a diffuse tumor had malignant gliomas grade III or IV (Table 1). Three of these patients died within 4 weeks of surgery, one of sepsis and meningitis and two of pulmonary complications. Four patients were more impaired postoperatively as a result of additional cranial nerve dysfunction. No patient was improved by surgery and all died from tumor progression within 6 to 12 months of surgery.

**Focal Tumor.** None of the four patients with focal tumor died or was permanently more impaired as a result of the procedure. One lesion was a malignant astrocytoma (grade III to IV) and three tumors were benign astrocytomas (grade I or II). The patient with a malignant tumor did not improve and died of tumor progression 6 months after surgery. One patient with a benign neoplasm recovered neurological function and is well 12 months after surgery. The other patients were severely disabled preoperatively and, although they are now stable, have not recovered significant neurological function.

**Cervicomedullary Tumor.** All eight patients with cervicomedullary neoplasms had benign astrocytomas (grade I or II). There was one operative mortality from meningitis and sepsis in a severely disabled patient 4 weeks following surgery. No patient became more impaired and six patients have made an excellent neuro-

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† Cordis Brain State Analyzer manufactured by Cordis Laboratories, Inc., P.O. Box 523580, Miami, Florida.

<table>
<thead>
<tr>
<th>Tumor Classification</th>
<th>No. of Cases</th>
<th>Pathological Grade</th>
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<tbody>
<tr>
<td>diffuse</td>
<td>22</td>
<td>all malignant (grades III–IV)</td>
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<tr>
<td>focal</td>
<td>4</td>
<td>3 benign (grades I–II)</td>
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<tr>
<td></td>
<td></td>
<td>1 malignant (grades III–IV)</td>
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<tr>
<td>cervicomedullary</td>
<td>8</td>
<td>all benign (grades I–II)</td>
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**FIG. 2.** Left: Sagittal reconstruction of a contrast-enhanced computerized tomography (CT) scan disclosing a cervicomedullary neoplasm. Center: Contrast-enhanced CT scan in another patient showing a tumor at the cervicomedullary junction. Right: Magnetic resonance imaging clearly delimits the rostral and caudal extent of a cervicomedullary junction tumor.
a few of these neoplasms may be cervical spinal cord tumors that have grown rostrally into the medulla, as the microscopic pathology is similar to typical low-grade astrocytomas that occur in the spinal cord. In other words, whereas the great majority of spinal cord astrocytomas of childhood are benign, the converse is the situation in the pons and midbrain where the overwhelming number of neoplasms are highly malignant.3 Tumors of the cervicomedullary junction may represent a "melting pot" in terms of the pathology, and perhaps primary surgical extirpation will be most applicable to tumors in this location.

Although surgery has been reasonably well tolerated and the patients with low-grade astrocytomas are doing well in a short follow-up period, we are not recommending that all potentially benign neoplasms be excised. The experience to date is much too limited and, with the exception of tumors of the cervicomedullary junction, it seems clear that radiation therapy usually remains the most effective therapy. Surgery may be considered at some time after radiation if a lengthy survival, a focal neoplasm, and an insidious course indicate a benign neoplasm.

Some authors have suggested that it is important to perform routine biopsy of brain-stem tumors so as to make an accurate pathological diagnosis prior to recommending a course of treatment.1,5 We take strong exception to this because there is no consistent useful information to be obtained from biopsy and the fact that a procedure may be carried out with little morbidity and mortality does not justify inflicting it on an already ill child. It must be recognized that the microscopic pathology of a brain-stem tumor is not homogeneous. Glioblastomas commonly have a large component which, if examined alone, would be diagnosed as a grade II astrocytoma. The only situation in which a brain-stem biopsy is meaningful is when it discloses a highly malignant tumor, in which case the biology of the neoplasm will be related to its most malignant component and the dismal prognosis will be obvious. However, in cases in which biopsy discloses a low-grade neoplasm, there is no way of assessing whether or not this reflects the microscopic pathology of the center of the neoplasm, and it is not logical to recommend a treatment course based on that examination. In fact, in our experience with radical excision of brain-stem neoplasms we have operated on two cases in which a relatively large surgical specimen revealed a grade II astrocytoma while the autopsy specimen (12 days and 36 days postoperatively) disclosed classical local and disseminated glioblastomas.

It is intriguing that a few patients with apparent brain-stem neoplasms continue to survive many years after diagnosis. It seems likely that in some of these cases the diagnosis was made prior to the availability of computerized tomography, and that some of these good results were in children who had an incorrect diagnosis. Our own experience supports this hypothesis inasmuch as we encountered two pontine hematomas secondary to logical recovery. Two severely disabled patients are neurologically stable 12 and 24 months postoperatively (Fig. 3).

**Discussion**

This series suggests that surgery is potentially beneficial only for benign astrocytomas (grade I or II) of the brainstem. No patient with a malignant tumor was significantly benefitted and all died within 12 months of surgery. Therefore, if a surgical option is to be seriously considered, it is essential that there be some relatively reliable preoperative assessment of the tumor pathology. Perhaps the observation of pathology vis-à-vis the clinical course and neurodiagnostic assessment of the extent of tumor may be pertinent in making this evaluation. All diffuse neoplasms were associated with typical symptomatology and were malignant. Diffuse edema was found in all cases of highly malignant tumors, even when the enhancing portion was small and circumscribed. This observation suggests that what appears to be edema may in fact be infiltrating neoplasm. Perhaps MRI will make this differentiation possible in the future.

Of the four focal tumors, three were low-grade astrocytomas. The patient with a focal but malignant tumor had a clinical course typical of brain-stem astrocytoma, while those with benign tumors had minimal early signs and symptoms, which were only slowly progressive. Therefore, it would seem that a focal neoplasm associated with a paucity of neurological signs and symptoms may be benign while the tumors that have a similar appearance but are associated with bilateral cranial nerve dysfunction and long-tract signs are malignant.

Perhaps the most important observation in this series of patients was that all of the cervicomedullary neoplasms were low-grade astrocytomas. It is possible that a few of these neoplasms may be cervical spinal cord neoplasms, even when the enhancing portion was small and circumscribed. This observation suggests that what appears to be edema may in fact be infiltrating neoplasm.

FIG. 3. Magnetic resonance imaging in a patient with a cervicomedullary tumor. Left: Diffuse expansion of the medulla and rostral spinal cord can be seen on the preoperative scan. Right: Six months postoperatively there is significant improvement in the appearance of both the medulla and spinal cord.
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to an occult angioma and one arachnoid cyst of the
civus, all of which had been misinterpreted as intrinsic
brain-stem neoplasms. This emphasizes the necessity of
expert review of technically satisfactory neurodiagnostic
studies, as the correct diagnosis was obvious retro-
spectively, and with proper neuroradiological attention
misinterpretation would not have occurred.

Summary

We have classified intrinsic brain-stem neoplasms as
diffuse, focal, and cervicomedullary. In 34 patients,
pathological examination following radical tumor ex-
cision revealed that all of the diffuse tumors and one
of the focal tumors were malignant astrocytomas (grade
III or IV), and all of the cervicomedullary neoplasms
were low-grade astrocytomas (grade I or II). Although
surgery was relatively well tolerated, no patient with a
malignant tumor benefitted from the procedure. With
one exception, the patients with benign neoplasms
either were stabilized or improved after surgery. It is
concluded that patients with neoplasms of the cervico-
medullary junction may be improved through surgery.
Tumors rostral to the medulla are almost all malignant,
although it is possible that focal tumors with little
neurological dysfunction may be benign. Nevertheless,
in this latter group of patients radiation therapy remains
the treatment of choice until additional surgical expe-
rience and long-term follow-up results are available.

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