Diagnosis and management of pediatric brain-stem gliomas

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The authors reviewed the cases of 49 children, ranging in age from 9 months to 15 years, who were diagnosed by computerized tomography (CT) as having brain-stem glioma. Four distinct groups of brain-stem gliomas were identified based on CT scan characteristics: Group I included isodense contrast-enhancing tumors that were dorsally exophytic into the fourth ventricle; Group II(a) included hypodense nonenhancing intrinsic tumors of the brain stem; Group II(b) included intrinsic tumors of the brain stem with hyperdense exophytic components extending ventrally and laterally into the cerebellopontine and preoptic cisterns; Group III included intrinsic cystic tumors with contrast-enhancing capsules; and Group IV included focally intrinsic tumors of the brain stem that were isodense and enhanced brightly on administration of contrast medium.

The clinical presentation, efficacy of surgical intervention, pathology, and prognosis of these tumors were correlated within these groupings. Eleven patients had Group I tumors, all of which were surgically resected; 10 of the 11 lesions were proven to be low-grade gliomas. These patients had an excellent prognosis; 10 of the 11 survived, with a mean follow-up period of 4.5 years. There were 18 patients with Group II(a) tumors; although tumor biopsy was attempted on eight of these, pathological diagnosis at the time of surgery was made in only one case. These patients did poorly; the mean survival time was 6.2 months. The seven Group II(b) tumor patients demonstrated a similarly poor prognosis: all of them died within 23 months of diagnosis, with a mean survival time of 12 months. Only two of six patients undergoing biopsy had sufficient tissue for histological verification. Three of the four patients with Group III tumors died; their mean survival time was 11.5 months. Successful histological examination was carried out in all four cases. The nine Group IV tumor patients did reasonably well; seven of these patients remain alive, with a mean follow-up period of 2.3 years. Histological diagnosis was obtained in three of the seven patients who were explored in this group. This classification system has proven to be of value in determining prognosis and efficacy of surgical intervention.

KEY WORDS • astrocytoma • brain tumor • brain-stem tumor • glioblastoma • classification system • computerized tomography • children

Brain-stem gliomas are common childhood tumors and account for some 10% to 25% of all intracranial childhood tumors.4,5,10,16 Recent reports suggest that brain-stem gliomas are just as common as the medulloblastomas and cerebellar astrocytomas.3 Despite their relatively common occurrence, the management of this type of tumor remains controversial. This in part relates to the fact that these tumors behave quite differently from one another in terms of growth and prognosis.6 Some authors have attributed these differences to the location of the tumor within the brain stem.1,15,16

In an effort to clarify the biological behavior of these neoplasms, we have reviewed the cases of 49 patients with brain-stem tumors who were managed at The Hospital for Sick Children, Toronto, since the computerized tomography (CT) scanner became available (1976 to 1985). The tumors were categorized according to CT appearance as well as by clinical symptomatology and outcome in order to assess the prognosis and to determine management.

Clinical Material and Methods

In the 10-year period from 1976 to 1985, during which CT scanning was utilized for evaluating all brain tumors at The Hospital for Sick Children, Toronto, 49 patients ranging in age from 9 months to 15 years were diagnosed as having a brain-stem glioma. These patients consisted of 31 girls and 18 boys, and presented with histories of between 3 days and several years. These
patients were grouped on the basis of the location of the tumor; whether it was intrinsic or extrinsic to the brain stem; parenchymal features such as whether the tumor was solid or cystic; and the contrast-enhancing CT features of the tumors.

Group I: Tumors that were isodense or slightly hypodense and were dorsally exophytic from the brain stem into the fourth ventricle. They enhanced brightly on post-contrast CT scans (Fig. 1).

Group II(a): Intrinsic brain-stem tumors that were hypodense and did not enhance on CT scans after administration of contrast medium (Fig. 2 left).

Group II(b): Intrinsic brain-stem tumors that had hyperdense, exophytic, contrast-enhancing components extending into the cerebellopontine and prepontine cisterns (Fig. 2 right).

Group III: Cystic tumors with contrast-enhancing capsules that were situated focally within the brain stem (Fig. 3 left).

Group IV: Focal tumors intrinsic to the brain stem which were isodense and contrast-enhanced brightly (Fig. 3 right).

We correlated this classification scheme with symptoms and signs, efficacy of surgical treatment, and prognosis in the 49 patients.

Thirty-five (71%) of the 49 patients underwent a suboccipital craniectomy for histological evaluation, decompression, subtotal resection of the tumor, and/or cyst aspiration. One patient was subjected to subtemporal exploration of a cystic tumor within the brain stem. Histological diagnosis was established in 21 (58%) of the 36 patients. However, the efficacy of these procedures and the chance of establishing a histological diagnosis varied greatly among the different groups, which in turn differed greatly with regard to prognosis.

Summary of Cases

Table 1 summarizes the CT and histological findings in each group of tumors in relation to outcome.

Group I Tumors

Eleven patients had Group I tumors. These patients ranged in age between 18 months and 12 years and included seven girls and four boys. The symptoms were typically insidious and of longer duration than those of other brain-stem tumors. Failure to thrive was seen in the three youngest patients who were all under 2 years of age. Hydrocephalus varying from mild to severe ventricular dilatation was a common feature and was seen in six of the 11 patients. Ataxia was present in
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TABLE 1
Summary of computerized tomography (CT) and histological findings in relation to outcome

<table>
<thead>
<tr>
<th>Group</th>
<th>CT Characteristics</th>
<th>Definitive Histology</th>
<th>No. of Cases</th>
<th>Outcome*</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>dorsally exophytic tumor</td>
<td>grade I–II astrocytoma grade III astrocytoma ganglioglioma</td>
<td>9</td>
<td>10/11 alive: mean follow-up period 4.5 yrs</td>
</tr>
<tr>
<td>II(a)</td>
<td>diffuse intrinsic, nonenhancing tumor</td>
<td>grade III astrocytoma glioblastoma multiforme</td>
<td>3</td>
<td>0/18 alive: mean survival time 6.2 mos</td>
</tr>
<tr>
<td>II(b)</td>
<td>diffuse intrinsic enhancing tumor, with exophytic components</td>
<td>grade III astrocytoma glioblastoma multiforme</td>
<td>3</td>
<td>0/7 alive: mean survival time 12 mos</td>
</tr>
<tr>
<td>III</td>
<td>focal intrinsic cystic tumor</td>
<td>grade I–II astrocytoma grade III astrocytoma</td>
<td>2</td>
<td>1/4 alive; follow-up period 8 mos</td>
</tr>
<tr>
<td>IV</td>
<td>focal intrinsic solid tumor</td>
<td>grade I–II astrocytoma grade III astrocytoma</td>
<td>2</td>
<td>7/9 alive: mean follow-up period 2.3 yrs</td>
</tr>
</tbody>
</table>

* Number of patients alive/total patients in that group. Mean follow-up time is given for the survivors.

TABLE 2
Presenting features in 49 cases of brain-stem gliomas

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Cases</th>
<th>Age Range (yrs)</th>
<th>Sex (F:M)</th>
<th>Hydrocephalus</th>
<th>Cranial N. Deficits</th>
<th>Long-Track Signs</th>
<th>Ataxia</th>
<th>Failure to Thrive</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>11</td>
<td>1–12</td>
<td>7:4</td>
<td>6</td>
<td>2</td>
<td>0</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>II(a)</td>
<td>18</td>
<td>4–13</td>
<td>8:10</td>
<td>7</td>
<td>16</td>
<td>13</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>II(b)</td>
<td>7</td>
<td>2–8</td>
<td>6:1</td>
<td>1</td>
<td>7</td>
<td>6</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>III</td>
<td>4</td>
<td>3, 4, 7, &amp; 15</td>
<td>2:2</td>
<td>2</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>IV</td>
<td>9</td>
<td>4–15</td>
<td>8:1</td>
<td>2</td>
<td>7</td>
<td>5</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

eight patients. Cranial nerve deficits and long-tract signs were uncommon in comparison with their more frequent presentation in other types of brain-stem gliomas (Table 2).

All 11 patients underwent subtotal resection of their tumors via a suboccipital craniectomy. Perioperative shunting was performed in eight of these patients. Two received ventriculoperitoneal (VP) shunts prior to suboccipital craniectomy, and six had cannulation of the aqueduct of Sylvius at the time of the posterior fossa exploration. Two patients required postoperative shunts. At surgery, all 11 patients demonstrated a mass fungating out of the dorsum of the brain stem, breaching the ependyma of the floor of the fourth ventricle, and largely filling the fourth ventricle (Fig. 1). Ten tumors were solid and one was cystic. Subtotal resection was performed using microsurgical techniques and in more recent years the Cavitron ultrasonic apparatus, leaving a residual carpet of tumor on the floor of the fourth ventricle whence these tumors arose.

Histological evaluation was obtained in all 11 patients. Nine patients had grade I or II astrocytomas, one patient had a grade III astrocytoma, and one had a ganglioglioma. The one patient with a relatively high-grade glioma received postoperative radiotherapy. Two of the other 10 patients subsequently received radiotherapy because the residual tumor showed evidence of growth on routine follow-up CT scans.

One patient died of shunt malfunction in another institution 18 months after the initial tumor diagnosis was made. Two patients did not receive irradiation, and showed no residual tumor on follow-up CT scans (Fig. 4). Six patients have tumors that have not shown any evidence of growth following subtotal resection. Of the two patients who received radiotherapy, one had no tumor on his latest CT scan. The patients in Group I

FIG. 4. Enhanced computerized tomography scans in a patient with a Group I brain-stem tumor. *Left:* Scan obtained prior to resection. *Right:* Follow-up scan 4 years after subtotal resection showing no residual tumor. Note the catheter in the fourth ventricle which runs from the third ventricle into the cisterna magna.
have enjoyed an excellent outcome; the follow-up time ranged from 9 months to 9 years, with a mean follow-up period of 4.5 years and a median follow-up time of 4 years.

**Group II(a) Tumors**

Eighteen patients (eight girls and 10 boys), ranging in age from 9 months to 13 years, had Group II(a) tumors. Duration of symptoms ranged from a few days to several months. Cranial nerve deficits and long-tract signs were common in this group of patients while hydrocephalus and ataxia were relatively rare, in contrast to the Group I tumor patients (Table 2).

Eight of these 18 patients underwent a suboccipital craniectomy for tumor biopsy. In only one patient was the biopsy adequate to establish a histological diagnosis of grade I to II astrocytoma, and this diagnosis was probably inaccurate as the patient died 7 months later. Although no postmortem examination was performed, the rapid progression of his tumor conformed with the pattern of a much more malignant growth. The remaining seven biopsies yielded nondiagnostic tissue.

The prognosis for these patients is dismal: none in this group survived beyond 20 months from the time of diagnosis. Although radiotherapy and chemotherapy seemed to prolong life, they were not curative. Six patients who received no radiotherapy survived between 1 week and 4 months, with a mean survival time of 9.5 weeks. Of the 12 patients receiving radiotherapy, survival times ranged from 4 to 20 months, with a mean survival period of 8.5 months.

Postmortem examinations were performed on six of these 18 patients, three of whom had had nondiagnostic needle biopsies. Three patients had a grade III astrocytoma and three had a glioblastoma multiforme. The tumors were variable in their malignancy, depending on which region or section of tumor was viewed, which may explain why biopsies can be unsuccessful in establishing an accurate diagnosis. Four of the six tumors demonstrated evidence of subarachnoid spread at the time of autopsy.

**Group II(b) Tumors**

Seven patients had Group II(b) tumors. It is of interest that several patients with Group II(a) tumors showed the appearance of a Group II(b) tumor during the course of their management following treatment (Fig. 5); however, in the case of these seven patients, a Group II(b) appearance was present at the time of initial management in our institution. These children (six girls and one boy) ranged in age from 2 to 8 years. Cranial nerve deficits and long-tract signs were common features, whereas hydrocephalus and ataxia were rare (Table 2). Six of the seven patients had a suboccipital exploration and a histological diagnosis was obtained in two: one a grade I to II astrocytoma and one a grade III astrocytoma. Both biopsy specimens were nondiagnostic.

As with Group II(a) tumors, the prognosis was dismal and none of these patients survived beyond 23 months. One patient who was not irradiated died within 3 days of initial presentation. The remaining six received radiotherapy and survived between 6 to 23 months, with a mean survival time of 12 months. The one patient in this group who had a postmortem examination had a glioblastoma multiforme with diffuse subarachnoid spread.

**Group III Tumors**

Four patients (two girls and two boys) had Group III tumors, which were cystic and intrinsic to the brain stem. These patients were 3, 4, 7, and 15 years of age. All four patients exhibited cranial nerve deficits and long-tract signs, and two of the four patients had hydrocephalus requiring VP shunting (Table 2). Three patients underwent a suboccipital craniectomy and one a subtemporal craniotomy for biopsy and drainage of their cysts. Two patients had grade I to II astrocytomas, and two had malignant astrocytomas. All four patients underwent radiotherapy. Three have died, with survival periods of 1, 13, and 20 months. The one patient remaining alive has survived for 8 months and is in poor condition at the present time.

**Group IV Tumors**

Nine patients had Group IV tumors, which were isodense and contrast-enhancing lesions focally intrinsic to the brain stem. These patients were 4 to 15 years of age and included eight girls and one boy. Cranial nerve deficits and long-tract signs were common. Hydrocephalus and ataxia were relatively uncommon (Table 2). Seven of these nine patients underwent a posterior fossa exploration and biopsy. Histological findings...
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diagnosis was established in three patients: two had low-grade astrocytomas and one a malignant astrocytoma. In four patients, the tissue yielded was considered inadequate for diagnosis.

Eight of these nine patients received radiotherapy. The one patient without irradiation is alive, having survived for 6 years. Two patients have died: one 3 months and one 6 years after initial treatment. The remaining seven patients have now survived between 10 months and 6 years, with a mean follow-up period of 2.3 years.

Discussion

Modern imaging has greatly enhanced the preoperative evaluation of brain-stem tumors. Prior to 1976, pneumoencephalography and angiography were used at our institution for definition of posterior fossa lesions. Although these diagnostic techniques provided clues as to mass size and occasionally as to exophytic components of brain-stem tumors, clarification of the detailed nature of the tumors was not possible until the development of high-resolution CT imaging. Magnetic resonance imaging should further improve our diagnostic capability. With the availability of these imaging tools, we have been able to identify differences among tumors that in the past were considered and treated as a single entity.

Matson concluded that exploration for histological confirmation of brain-stem tumors should be avoided because the outcome was invariably poor: "Regardless of specific histology, brainstem gliomas must be classified as malignant tumors since their location in itself renders them inoperable." Computerized tomography has allowed us to differentiate the various brain-stem tumors, allowing for the comparison of anatomical location and characteristics with presentation, surgical efficacy, and prognosis.

Group I brain-stem tumors arise in the floor of the fourth ventricle and grow exophytically into the fourth ventricle. We suspect that actual brain-stem infiltration is limited in comparison with truly intrinsic components of brain-stem tumors because of the intrinsic nature of these tumors. Confirmation of brain-stem tumors should be avoided because the outcome was invariably poor: "Regardless of specific histology, brainstem gliomas must be classified as malignant tumors since their location in itself renders them inoperable." Computerized tomography has allowed us to differentiate the various brain-stem tumors, allowing for the comparison of anatomical location and characteristics with presentation, surgical efficacy, and prognosis.

Group I brain-stem tumors tend to have low-grade tumors which were intrinsic to a focal part of the brain stem, usually at the cervicomedullary junction. Several of these patients have survived for long periods of time. We feel that radiotherapy has a role to play in this particular group of tumors.

Conclusions

This classification of brain-stem tumors, which is based on neuro-imaging, can help the surgeon not only to determine which cases will benefit from surgery, but also to assess the prognosis. All patients with Group I tumors should undergo subtotal resection of the lesion, and radiotherapy should be limited to those patients who develop regrowth of tumor on follow-up scans. The patients with Group II tumors carry a poor prognosis. Surgical biopsy has been of little value for this group in our hands. Radiotherapy and chemotherapy may prolong survival time, but have not been curative. The patients with Group III tumors are amenable to cyst aspiration and surgical biopsy; however, in our small number of patients with Group III tumors, the outlook has been poor. The patients with Group IV tumors tended to have low-grade astrocytomas, usually at the cervicomedullary junction, many of which can be partially resected. Because of the intrinsic nature of these tumors, it is impossible to carry out a radical resection, and radiotherapy seems to have a beneficial effect on the residual tumor.

References

1. Abramson N, Raben M, Cavannaugh PJ: Brain tumors in


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