Surgical treatment of brain stem gliomas

KENNETH R. L. LASSITER, M.D., EHEN ALEXANDER, JR., M.D., COURTLAND H. DAVIS, JR., M.D., AND DAVID L. KELLY, JR., M.D.
Department of Surgery, Section on Neurosurgery, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, North Carolina

A long-term study has been made of a consecutive series of 37 patients with brain stem gliomas, 22 of whom were children and 15 adults. Surgical exploration was carried out in 34 of the 37 cases and only very rarely was a diagnosis made on clinical grounds or air study alone. In 10 cases a histological diagnosis was made at operation. In five patients a significantly large neoplastic cyst was found and evacuated, and four of these have had long-term useful survivals. There were nine postoperative deaths, most of them in the pre-Decadron era; 17 cases died during follow-up, with a mean survival of 33 months; and eight patients are living, with a mean survival of 3 months to 9 years. A plea is made for surgical exploration of these lesions in the hope of finding a surgically approachable cyst, and for the use of radiation therapy at a later time.

KEY WORDS. brain tumor · brain stem glioma · cystic glioma

IN 1939, Bailey, et al.,² described the treatment of brain stem gliomas as "a pessimistic chapter" in the history of neurosurgery. Because of the anatomical location and the tendency to infiltrate along fiber tracts, the early signs and symptoms of brain stem glioma are frequently misleading. This insidious development in the absence of papilledema makes early diagnosis difficult.⁶ Once diagnosed, radiation therapy alone is at best palliative.⁵,4,15 For this reason we have attempted to analyze the value of surgical exploration prior to radiation therapy in this generally discouraging group of patients.

Case Material

From January, 1950, to January, 1970, we have treated 37 patients with brain stem gliomas at the North Carolina Baptist Hospital. As outlined in Table 1, one patient entered the hospital neurologically deteriorated and was given radiation therapy after the diagnosis of brain stem glioma was made by air study. Two additional patients died shortly after admission to the hospital, and postmortem examination confirmed the presence of pontine glioma. Thirty-four patients had surgical exploration after the diagnosis of brain stem glioma was made or suspected by air study.

In our consecutive series of 37 patients, there were 22 children and 15 adults. There were 20 females and 17 males. The age of onset of symptoms ranged from 6 months to 61 years. The average age in the pediatric group was 7 years and in the adult group 35 years. The average duration of symptoms for children was less than 2 months, while the adult group averaged 8 months. Gait disturbance and headache were the most common symptoms described by the patient at the time of initial examination (Table 2). These were followed closely by localized weakness and diplopia.

Initial clinical examination typically revealed involvement of multiple cranial nerves (Table 3). The most commonly affected were the sixth and seventh cranial nerves.
TABLE 1

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>radiation therapy</td>
<td>1</td>
</tr>
<tr>
<td>no treatment</td>
<td>2</td>
</tr>
<tr>
<td>exploration &amp; radiation</td>
<td>34</td>
</tr>
<tr>
<td><strong>total</strong></td>
<td><strong>37</strong></td>
</tr>
</tbody>
</table>

nerves. In 10 instances, these nerves were involved bilaterally. The complete triad of multiple cranial nerve involvement, ataxia, and pyramidal tract signs was present in 30 of the patients. Only one patient had papilledema at the time of initial examination.

In six of the patients who were explored before radiation therapy, it was possible to take a biopsy safely or to remove subtotally the tumor which protruded into the fourth ventricle or fungated anterolaterally from the pons.

In five additional patients, large neoplastic cysts in the brain stem were evacuated by needle aspiration. Because of the unusual operative findings and clinical course of these five patients, they are presented in more detail.

**Case Reports**

**Case 1**

A 14-year-old boy was admitted to the neurosurgical service on June 17, 1961, with a chief complaint of unsteady gait of 4 weeks’ duration. About 1 month before admission, he had noted the gradual onset of unsteady gait and clumsiness of the right hand. He had no other symptoms. Approximately 4 days before admission, the ataxia increased in severity.

**Examination.** The patient was alert and cooperative. He had horizontal nystagmus on lateral gaze. There was no papilledema. The corneal reflex was diminished on the right. The gag reflex was absent, and the uvula was deviated to the left. He had no motor or other sensory deficit. The plantar reflexes were flexor. He had a pronounced ataxic gait and had difficulty in turning. The Romberg sign was positive. Finger-to-nose testing was performed poorly on the right. The cerebrospinal fluid was clear and under normal pressure. A pneumoencephalogram showed elevation of the aqueduct and fourth ventricle with a shift of these structures to the left.

**Operation.** A posterior fossa exploration was performed, and a large cystic tumor was seen presenting laterally from the pons. Twelve cc of straw-colored fluid were aspirated from the cyst (Fig. 1). A nodule of tumor within the cyst was removed subtotally, and a modified Torkildsen’s shunt was left in place. The histological diagnosis was astrocytoma.

**Postoperative Course.** Recovery was uncomplicated, and the patient was given 4500 R over the next 6 weeks. The ataxia improved slowly following radiation therapy. His neurological status was stable until February, 1963, when he again became ataxic. He was given another 2000 R at the Medical College of Virginia. Following this therapy, he improved greatly. A recent examination at the North Carolina Baptist Hospital revealed only bilateral lateral nystagmus. He has since finished college and now, 8½ years after the initial operation, is in good health and pursuing a career.

**TABLE 2**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>gait disturbance</td>
<td>27</td>
</tr>
<tr>
<td>headache</td>
<td>21</td>
</tr>
<tr>
<td>localized weakness</td>
<td>18</td>
</tr>
<tr>
<td>squint or diplopia</td>
<td>17</td>
</tr>
<tr>
<td>personality change</td>
<td>16</td>
</tr>
<tr>
<td>facial weakness</td>
<td>11</td>
</tr>
<tr>
<td>drowsiness</td>
<td>9</td>
</tr>
<tr>
<td>facial numbness</td>
<td>5</td>
</tr>
<tr>
<td>vomiting</td>
<td>5</td>
</tr>
<tr>
<td>speech defect</td>
<td>2</td>
</tr>
<tr>
<td>decreased hearing</td>
<td>1</td>
</tr>
</tbody>
</table>

**TABLE 3**

<table>
<thead>
<tr>
<th>Cranial Nerve</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>VII</td>
<td>27</td>
</tr>
<tr>
<td>VI</td>
<td>24</td>
</tr>
<tr>
<td>V (sensory)</td>
<td>18</td>
</tr>
<tr>
<td>IX and X</td>
<td>9</td>
</tr>
<tr>
<td>XII</td>
<td>6</td>
</tr>
<tr>
<td>III</td>
<td>4</td>
</tr>
<tr>
<td>VIII</td>
<td>4</td>
</tr>
<tr>
<td>XI</td>
<td>2</td>
</tr>
</tbody>
</table>
Surgical treatment of brain stem gliomas

Fig. 1. Diagrams showing location of cysts related to brain stem glioma in five cases. The shaded area represents part of the brain stem noted to be abnormal by the surgeon. Needle aspirations were performed through these areas.

since diagnosis, he works for a department store.

Case 2

A 5-year-old boy was admitted to the North Carolina Baptist Hospital in December, 1960, with a 4-month history of right hemiparesis. A pneumoencephalogram was negative. The right hemiparesis progressed, and he was admitted to the neurosurgical service in June, 1961.

First Examination. The patient was lethargic and irritable. There was a right facial weakness and weakness of the right trapezius. He had a right hemiparesis and a Babinski sign. There was no papilledema. An arteriogram was negative. Pneumoencephalogram revealed displacement of the aqueduct to the right.

First Operation. A temporooccipital craniotomy was performed. When the tentorium was incised, a bluish mass was seen in the left mesencephalon. A needle was inserted, and 12 cc of yellow fluid were removed (Fig. 1).
1). The cyst was entered and a small nodule of tumor removed. A modified Torkildsen's shunt was done. The histological diagnosis was astrocytoma.

First Postoperative Course. The patient received no radiation therapy postoperatively. He did well with a mild residual hemiparesis until January, 1969. At that time he was readmitted with increasing right hemiparesis and headache.

Second Examination. The patient was alert and cooperative. In addition to the right hemiparesis with a right Babinski sign, he had left dysmetria, right facial weakness and numbness, and an absent gag reflex. There was a left internuclear opthalmoplegia and absence of upward gaze. A left retrograde brachial angiogram showed lateral displacement of both posterior cerebral arteries (Fig. 2). Pneumoencephalogram failed to outline structures in the posterior fossa. There was no hydrocephalus.

Second Operation. A bluish discoloration was again seen laterally in the left midbrain. Above the level of the posterior cerebral artery, a needle was inserted into the midbrain and 27 cc of yellow fluid removed (Fig. 1).

Second Postoperative Course. The patient tolerated the operation well and received a course of radiation postoperatively. She made a good recovery with considerable improvement in strength on the left. At age 5 she received another course of radiation therapy because of recurrent pain in the head and neck. Again she made a good recovery until the age of 7 when she was readmitted with ataxia, nystagmus, and headache.

Second Examination. The patient had bilateral papilledema and bilateral fifth cranial nerve palsy. A ventriculogram revealed di-

---

Case 3
This 6-month-old girl was admitted to the neurosurgical service with a 3-month history of irritability and weakness of the left arm and leg. The parents also had noted a tilt of the head to the left.

First Examination. The infant was found to have nuchal rigidity and a left hemiparesis. A myelogram revealed a complete block in the upper cervical region.

First Operation. A cervical laminectomy was performed from C-1 through C-7. The spinal cord at C-7 was normal but gradually widened up to the level of the foramen magnum. A posterior fossa exploration was then carried out. A large rounded mass was found protruding from the medulla in the region of the obex and extending into the upper cervical cord. A biopsy was taken and the histological diagnosis was astrocytoma.

First Postoperative Course. The patient tolerated the operation well and received a course of radiation postoperatively. She made a good recovery with considerable improvement in strength on the left. At age 5 she received another course of radiation therapy because of recurrent pain in the head and neck. Again she made a good recovery until the age of 7 when she was readmitted with ataxia, nystagmus, and headache.

Second Examination. The patient had bilateral papilledema and bilateral fifth cranial nerve palsy. A ventriculogram revealed di-
Surgical treatment of brain stem gliomas

lated lateral ventricles and a mass in the fourth ventricle.

Second Operation. A posterior fossa exploration was again performed. A large cystic tumor of the medulla and upper cervical cord was exposed. A 30 cc cyst was evacuated and the tumor removed subtotally (Fig. 1). A modified Torkildsen's shunt was performed.

Second Postoperative Course. The patient made a slow recovery and remained slightly ataxic. She gradually deteriorated over a 1-year period and died 13 years following diagnosis.

Case 4

An 8-year-old boy was first admitted to the North Carolina Baptist Hospital in May, 1952, with a 2-month history of unsteady gait. About 2 months before admission his parents had noted a disturbance of gait and a tendency to fall to the right. At about the same time they noted abnormal rapid movements of his eyes. Three weeks before admission headache and intermittent vomiting developed. The parents also noted that his voice had become high-pitched and nasal in quality.

First Examination. The patient was alert and cooperative. There was no papilledema. He had vertical and bilateral lateral nystagmus. A right facial weakness was noted. The gag reflex was absent, and the palate deviated to the left. The tongue deviated to the right. There were bilateral Babinski responses. He had no motor weakness. His gait was ataxic, and he had a left dysmetria. A pneumoencephalogram and ventriculogram failed to outline the aqueduct and fourth ventricle.

First Operation. A posterior fossa exploration was performed, and a large bluish mass was seen on the floor of the fourth ventricle. The brain stem was widened at the obex. A midline cyst was aspirated of 15 cc of yellow fluid (Fig. 1).

First Postoperative Course. Recovery was smooth. The patient received no radiation therapy. His neurological signs gradually cleared, and by November, 1953, physical examination was normal. He remained well until February, 1956, when he was readmitted with a 10-day history of vomiting without other symptoms.

Second Examination. The patient was noted to be slightly ataxic with a twelfth cranial nerve palsy. The plantar reflexes were flexor.

Second Operation. A posterior fossa exploration was again performed and a midline cyst evacuated from the brain stem. A grayish-pink tumor was removed subtotally from the cystic cavity. The histological diagnosis was astrocytoma.

Second Postoperative Course. The patient received two courses of radiation therapy during the next 3 years. He had clearing of all neurological signs after the first course and partial clearing after the second course. He deteriorated over a 4-month period and died of pneumonia 7\frac{1}{2} years following the original diagnosis.

Case 5

A 47-year-old man was admitted to the neurology service in September, 1969, with a 4-month history of weakness of the right arm and dysphagia. X-rays of the skull, radioisotopic brain scan, and lumbar puncture were negative. He was discharged and over the next 2 months developed diplopia, dysarthria, and progressive right hemiparesis.

Examination. When examined in November, 1969, the patient was oriented, cooperative, but apathetic. There was no papilledema. Bilateral lateral rectus palsy and failure of upward gaze were noted. The corneal reflex was absent on the right, and there was a right facial weakness. The gag reflex was absent, and the tongue deviated to the right. He had bilateral horizontal nystagmus and a left dysmetria. There was profound right hemiparesis with increased reflexes on the right. A repeat brain scan was negative. A left retrograde brachial arteriogram showed no abnormalities. A pneumoencephalogram showed upward and posterior displacement of the aqueduct and the fourth ventricle (Fig. 3).

Operation. A posterior fossa exploration was performed. The floor of the fourth ventricle was elevated and tilted to the right. A 25-gauge needle was inserted into the midline of the rhomboid fossa and 14 cc of yellow fluid aspirated (Fig. 1).

Postoperative Course. The patient tolerated the operation well and was given 5000 R over the next 5 weeks. He gradually im-
FIG. 3. Case 5. Pneumoencephalogram demonstrating symmetrical upward and posterior displacement of the aqueduct and fourth ventricle.

proved over the next 6 months, and then slowly deteriorated over a period of several weeks; he died approximately 1 year following diagnosis.

Discussion

Brain stem gliomas are more common in children than in adults and rarely occur under the age of 3 years. The youngest patient in our series was 6 months old. Luse and Teitelbaum recently reported a case of congenital pontine glioma. Their patient died because of respiratory failure at the age of 6 days; at postmortem examination a large malignant glioma was found in the pons.

The symptoms of brain stem glioma and their frequency in the present series vary little from those documented in the past. Ataxia, pyramidal tract signs, and deficits of multiple cranial nerves in the absence of papilledema dominated the clinical findings.

Our experience with the clinical response to radiation therapy is similar to that reported by other workers. Bray, et al., found a remarkable consistency in the time required for clinical improvement. Most of their patients showed improvement between 3 to 6 weeks after therapy was begun. They reported good improvement in 15 of 24 patients treated. Their patients who showed improvement following radiation therapy had an average survival time of 11.5 months. The patients who did not respond to therapy had a mean survival time of 4.5 months.

Lassman and Arjona reported a mean survival time of 15 months in the group that received radiation therapy compared to only 4 months in the group that received no therapy. There was good subjective improvement and objective clearing of neurological signs in 15 of the 16 children treated in our series. Only two of nine adults showed clearing of neurological signs following radiation therapy.

In Buckley's review of 25 cases of verified pontine glioma from Cushing's series, 10 were classified as glioblastoma multiforme, five as spongioblastoma unipolare, nine as astrocytoma, and one was unclassified. Alpers and Yaskin's series contained 10 cases classified as astrocytoma, three as spongioblastoma polare, and one as glioblastoma multiforme. In our series, histological examination was possible in 19 cases, either from surgery or by necropsy. Thirteen were astrocytoma and six glioblastoma multiforme.

The cystic nature of brain stem tumors was originally emphasized by Buckley. The presence of small cysts, even in highly malignant tumors, is not unusual (Fig. 4). Isolated cases of long-term survival following aspiration of brain stem cysts have been reported. The fact, however, that surgically significant cysts may occur with some regularity has not previously been discussed in the literature. The cysts in our five cases ranged from 12 to 30 cc in volume. The volume of the normal brain stem sectioned similar to that illustrated in Fig. 1 ranges from 25 to 30 cc (personal observation). It is not surprising that drainage of these cysts before radiation therapy usually resulted in clinical improvement.

FIG. 4. Sagittal section of the brain to illustrate multicystic nature of glioblastoma multiforme of the brain stem.
TABLE 4

Results of operative cases

<table>
<thead>
<tr>
<th>Postop Status</th>
<th>No. of Cases</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>postoperative deaths</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>follow-up deaths</td>
<td>17</td>
<td>33 mos (mean)</td>
</tr>
<tr>
<td>follow-up continuing</td>
<td>8</td>
<td>3 mos-9 yrs</td>
</tr>
</tbody>
</table>

As outlined in Table 4, there were nine postoperative deaths in the series of 34 operated cases. Six deaths occurred in adults who had deteriorated neurologically before operation. There has been no operative mortality since the advent of administering steroid therapy before and after operation. Of those patients who have since died, three patients lived 7½, 13, and 17 years. The mean survival of this entire group is 33 months. Eight patients in the series are still living. Three patients have exceeded 8 years of useful life since diagnosis. The remainder are still within 1 year of diagnosis.

In a review of our data, several important points emerge. At operation, a significant neoplastic cyst was found in five patients. Evacuation of this cyst has contributed to long-term survival in four of these patients. The fifth patient, an adult, made an initial good recovery following evacuation of the brain stem cyst, but slowly deteriorated over a period of several weeks and died approximately 1 year following diagnosis. The history, initial examination, and x-ray findings in these five patients were not unusual when compared to the remainder of the series. In 10 instances a histological diagnosis could be made at the time of operation. Because of the increased survival of those patients in whom a neoplastic cyst could be evacuated, surgical exploration of suspected brain stem gliomas should be considered before giving radiation therapy.

Summary

A series of 37 patients with brain stem gliomas has been surveyed, and the benefits of surgical exploration preceding radiation therapy evaluated in 34 cases. In 10 cases a histological diagnosis could be made at operation. In five cases a surgically significant neoplastic cyst of the brain stem could be aspirated. Patients with cysts improved neurologically following operation and before radiation. Aspiration of the brain stem cyst has contributed to long-term survival in four of the five cases presented.

References


Received for publication May 20, 1970.


Address reprint requests to: Eben Alexander, Jr., M.D., Department of Surgery, Section on Neurosurgery, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, North Carolina 27103.