Radiation of infratentorial and supratentorial brain-stem tumors

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A retrospective survey of 41 patients with unbiopsied thalamic, pontine, and medullary tumors treated with radiation therapy demonstrated 30% to 40% 3-year survival, with seven long-term survivors. Eleven of the 12 patients surviving over 3 years have essentially normal neurological function. Of seven patients in whom histological diagnoses were eventually obtained, four proved to have glioblastomas and three low-grade astrocytomas. Autopsy revealed that all glioblastomatous tumors extended beyond the treatment field; this suggested that larger volumes, perhaps the whole brain, should be irradiated. High doses (at least 5000 rads) should be used since the 3-year survival among those receiving such doses was 45%.

KEY WORDS • brain-stem tumors • radiation therapy

Tumors of the pons, medulla, and thalamus are usually treated with radiation therapy without biopsy, since taking a biopsy of the brain stem, whether infratentorial or supratentorial, entails a high risk. Only a few reports have been published regarding the radiation therapy of thalamic tumors; infratentorial or supratentorial, infratentorial brain-stem tumors have been investigated more often. This report is a retrospective review of the experience at the Mallinckrodt Institute of Radiology in the primary treatment of patients with infratentorial and supratentorial brain-stem tumors.

Clinical Material
From 1956 through December, 1972, 41 patients were seen at the institute with histologically unverified tumors of the brain stem diagnosed by clinical signs and symptoms, air study, and/or arteriogram. Seventeen patients were treated for supratentorial brain-stem tumors (thalamus) and 24 for infratentorial tumors (pons, medulla). The patients' ages ranged from 6 months to 68 years; 50% of the thalamic and an equal proportion of the pontine-medullary tumors became symptomatic between the ages of 9 and 34 years. Sixty percent of the thalamic and 40% of the pontine-medullary tumors occurred in patients under 16 years of age. Two patients with pontine tumors had received prior treatment; one had had a Holter valve inserted 3 years prior to radiation, and exploration with no biopsy immediately prior to radiation, while the other had received 3500 rads elsewhere 7 years and exploration without biopsy 5 years prior to treatment by radiation at our institution.
TABLE 1
Symptoms and signs in 41 patients with brain stem tumors

<table>
<thead>
<tr>
<th>Type of Tumor</th>
<th>Infratentorial (n = 24)</th>
<th>Supratentorial (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hemiparesis</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>headache, nausea, vomiting</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>cranial nerve abnormalities</td>
<td>19</td>
<td>3</td>
</tr>
<tr>
<td>ataxia</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>other cerebellar signs</td>
<td>12</td>
<td>3</td>
</tr>
</tbody>
</table>

TABLE 2
Value of diagnostic procedures in 41 patients with brain stem tumors*

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Type of Tumor</th>
<th>Infratentorial (n = 24)</th>
<th>Supratentorial (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ptyaumoencephalogram</td>
<td></td>
<td>17 (all +)</td>
<td>5 (4 +)</td>
</tr>
<tr>
<td>ventriculogram</td>
<td></td>
<td>2 (all +)</td>
<td>12 (11 +)</td>
</tr>
<tr>
<td>ptyaumoencephalogram and ventriculogram</td>
<td></td>
<td>5 (all +)</td>
<td>2 (1 +)</td>
</tr>
<tr>
<td>arteriography</td>
<td></td>
<td>9 (5 +)</td>
<td>11 (9 +)</td>
</tr>
<tr>
<td>brain scan</td>
<td></td>
<td>5 (1 +)</td>
<td>9 (5 +)</td>
</tr>
</tbody>
</table>

* + = positive test result.

Clinical Studies

Patients with pontine-medullary tumors almost invariably presented with cranial nerve symptoms, ataxia or other cerebellar abnormalities, and hemiparesis. The sixth and seventh cranial nerves were most commonly affected, followed by the fifth and tenth. Patients with thalamic tumors presented most commonly with hemiparesis and symptoms of increased intracranial pressure (Table 1). Air studies were performed on all patients with infratentorial tumors; 17 had pneumoencephalography, two ventriculography, and five both. All but one thalamic tumor were diagnosed by air study, 12 by ventriculography, and four by pneumoencephalography. Seven patients with infratentorial and 11 with supratentorial tumors had angiography prior to treatment. Only one of five brain scans performed on patients with infratentorial tumors was positive, and that tumor proved to be an arteriovenous malformation. Five of nine brain scans performed on patients with thalamic tumors were positive (Table 2).

Treatment

Surgery. Five cases of infratentorial and five of supratentorial tumors were treated with cerebrospinal fluid (CSF) shunting procedures prior to radiation. Four patients with infratentorial tumors were explored by a craniotomy prior to irradiation; the brain stem appeared enlarged in these cases; two were biopsied, but no tumor was present in the specimen. Two of these patients had been erroneously thought to have cerebellopontine angle tumors preoperatively. No thalamic tumors were explored prior to irradiation.

Radiation. Radiation therapy consisted of betatron 24-MeV x-rays in 24 patients, cobalt-60 gamma rays in 14, and 4-MeV linear accelerator x-rays in three. Four patients did not complete the planned radiation program because of death or clinical deterioration. Ports were most commonly round fields 8 cm in diameter or 8 x 12 cm rectangular fields, the size ranging from 6.5 x 7.5 cm to 10 x 12 cm. One infratentorial tumor was treated with whole brain and whole spine radiation and one thalamic tumor with whole brain radiation. All but two infratentorial tumors were treated with two opposing lateral fields. Six of the thalamic tumors were treated with a 4-field technique. The central axis midline depth dose ranged from 3000 to 5000 R; 76% of the patients received between 4500 and 5000 R. The usual fractionation was 160 rads tumor dose daily, five fractions per week.

Results

Two patients were lost to follow-up and are presumed dead due to tumor. Eight out of 24 patients with infratentorial tumors (33%) and six out of 17 patients with supratentorial lesions (43%) were considered clinically improved at the completion of radiation.

Three-Year Survival

Among the patients who completed radiation therapy and survived at least 3 years, 31% (six of 19) with infratentorial tumors and 43% (six of 14) with supratentorial tumors are still alive. Ten of the 12 3-year survivors now have either a normal neurological examination or some minor neurological abnormality (strabismus, minimal hemiparesis), and work regularly or attend schools or colleges. One patient, now 49 years old, who worked for 16
Radiation of brain stem tumors years following treatment, experienced what were thought to be two cerebrovascular accidents in the 17th year, with resulting aphasia and invalid status. One patient has been neurologically stable since treatment 4 years ago, but residual ataxia and sixth nerve palsy necessitate attendance at a school for the orthopedically handicapped. Two 3-year survivors were improved at the completion of radiation, six were symptomatically unchanged at the end of radiation but improved at 6 months, three were neurologically normal throughout radiation, and the immediate response of one patient to radiation is unknown.

In both groups, the 3-year survival rate for patients receiving 5000 rads or more was about 45% (Table 3). None of the 11 patients with infratentorial tumors who received less than 5000 rads survived 3 years. Survival of patients with supratentorial tumors was less well correlated with dose (Table 4).

Five Year Survival

There are seven 5-year survivors (12%); all are alive 6, 6, 8, 8, 9, 13, and 17 years after treatment. The 5-year survival rate for thalamic tumors was better than for infratentorial tumors (62% versus 14%). No difference in survival was seen among the limited variety of port sizes used. All deaths occurred within 3 years following treatment and half of them within 1 year of radiation (Fig. 1). There were no complications of treatment among the survivors.

Histological Verification

Histological diagnoses were made in six patients. Autopsies on three patients with infratentorial tumors showed two glioblastoma multiforme tumors and one Grade 2 astrocytoma, while autopsies on two patients with supratentorial tumors showed two glioblastoma multiforme tumors. The four glioblastomas proven at autopsy all extended beyond the brain stem. Extension into the occipital lobe meninges and corpus callosum was seen in one thalamic glioblastoma and extension into the pons and cerebellum in the other. The infratentorial glioblastomas at autopsy extended into the cerebellum, internal capsule, and midbrain in one case and into the meninges, midbrain, cerebellum, basal ganglia, and internal capsule in the other.

One thalamic glioblastoma and one infratentorial glioblastoma proved at autopsy to have meningeal tumor seeding of the cervical cord and cauda equina.

Two patients had supratentorial tumors that did not improve after radiation and subsequently underwent surgical resection. Grade 1 and Grade 2 astrocytomas were found; both patients died 4 months after surgery. One patient with an infratentorial tumor, whose hemiparesis cleared during radiation, developed a cranial bruit 1 year later and a brachial arteriogram, which had not been performed initially, showed a large arteriovenous malformation involving the brain stem, midbrain, and cerebellum. She is alive and asymptomatic 2½ years following radiation.

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**TABLE 3**

<table>
<thead>
<tr>
<th>Length of Survival (yrs)</th>
<th>Infratentorial (n = 24)*</th>
<th>Supratentorial (n = 17)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 6/19 31%</td>
<td>6/14 43%</td>
<td></td>
</tr>
<tr>
<td>5 2/14 14%</td>
<td>5/12 42%</td>
<td></td>
</tr>
<tr>
<td>10 1/7 14%</td>
<td>1/3 33%</td>
<td></td>
</tr>
</tbody>
</table>

* 23 of 24 patients completed radiation therapy. † 14 of 17 patients completed radiation therapy.

**TABLE 4**

<table>
<thead>
<tr>
<th>Dosage (rads)</th>
<th>Infratentorial</th>
<th>Supratentorial</th>
</tr>
</thead>
<tbody>
<tr>
<td>3000–4000</td>
<td>0/7</td>
<td>1/3</td>
</tr>
<tr>
<td>4100–4950</td>
<td>0/4</td>
<td>2/4</td>
</tr>
<tr>
<td>5000–6000</td>
<td>6/13</td>
<td>3/7</td>
</tr>
</tbody>
</table>

* Number of 3-year survivors/numbers of patients receiving given dosage.

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FIG. 1. Graph illustrating interval between radiation treatment and death in series of 41 patients.
Four patients received second courses of radiation of 2000 to 3000 rads between 12 and 17 months following initial treatment courses of 4000 to 5000 rads; all four died within a few months.

**Discussion**

Radiation therapists always feel uneasy when treating unbiopsied tumors. This study was undertaken partly to determine the histological diagnosis of treated unbiopsied brain stem tumors. The patient with an arteriovenous malformation demonstrates the necessity of angiography on all suspected brain tumors. Unfortunately, autopsies were performed on very few patients and in only seven of the 41 was a histological diagnosis made. Our finding two glioblastomas among the four proven thalamic tumors is similar to the 46%, 55%, and 57% incidences of glioblastomas that Cheek and Taveras, Tovi, et al., and McKissock and Paine found in 24, 22, and 7 seven proven thalamic tumors, respectively. Others have found four of 14, three of nine, six of 12, five of eight, seven of 10, and five of seven histologically proven pontine-medullary tumors to be glioblastomas, for an average of 42%. Two of the three histologically verified pontine or medullary tumors in our series were glioblastomas.

The high proportion of glioblastomas in clinically diagnosed brain-stem tumors raises the question of whether these tumors should be irradiated through large ports encompassing the whole brain as we and others have advocated for glioblastoma multiforme elsewhere, or through localized ports encompassing only the known tumor. Although it is unlikely that enlarging the ports would lead to increased curability or longer survival among patients with glioblastomas, it might well prolong life and delay progression of symptoms, since at autopsy all the tumors extended beyond the brain stem. On the other hand, many of the long-term survivors with low-grade astrocytomas are children, some of whom may live long enough to develop complications from radiation of additional areas of normal brain, scalp, and skull.

Patients with brain-stem tumors should be treated with high doses, at least 5000 rads, since the goal of treatment is a cure. Our results have further confirmed the findings of others that long-term survivals are definitely possible. Our 5-year survival rate of 12% does not equal that in several other series, namely 30%, 30%, and 38%; however, the majority of our survivors now have normal or nearly normal function, and are quite able to lead useful lives.

**References**


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