Oligodendrogliomas
An Analysis of 63 Cases

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We are reporting an analysis of 63 cases of oligodendroglioma studied and treated at the Montreal Neurological Institute. These comprise 2.7% of the total series of brain tumors at this institution.

Clinical Features

Seizures. The most common initial symptom (79%) in the series was seizure. In this group the average preoperative duration of symptoms was 7.3 years and the postoperative survival 5 years, compared to 2.5 and 6.8 years respectively in those who did not have seizures. Eleven percent had headaches, 3% weakness, and 3% mental changes. Forty-eight percent had hemiparesis, 39% papilledema, and 31% mental changes on the first admission. Only one patient had no signs.

Radiological Studies. Ventriculograms correctly diagnosed and localized the tumor in 100% of 25 cases tested; they were done on patients who had evidence of raised intracranial pressure, 75% of whom showed papilledema.

Pneumoencephalograms localized the tumor in 57% of 30 studies; there was no evidence of pressure or papilledema in any of the patients studied by pneumoencephalography. In several cases the pneumogram was misinterpreted as showing atrophy on the side contralateral to the tumor; in none of these was there a shift of the midline structures.

Angiography was carried out in 22 cases 73% of which showed some abnormality. No angiogram demonstrated pathological vessels, tumor blush, or early filling of tumor veins.

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Electroencephalography. The EEG was abnormal in 89% of 47 cases. It consisted of a slow-wave focus in 51% and a slow-and-sharp-wave disturbance in 49%, and had localizing value in 83% of the abnormal group.

Brain Scans. Brain scans were carried out on 18 patients using an automatic contour device with Hg-197 or Hg-203. The differential activity from corresponding areas on opposite sides of the head was compared quantitatively.

There was a wide variation in the degree of differential uptake over the tumors. The presence or absence of uptake, and its intensity, did not correlate with survival.

Lactic-Dehydrogenes Isoyme Pattern. This pattern was determined in two cases; in one it was that of a malignant glioma, in the other, that of a normal brain.

Fluid Protein Content. The lumbar or ventricular cerebrospinal fluid protein was not significantly elevated in the 37 cases in which it was measured. The protein content of the cyst fluid approximated that of serum in nine cases. The electrophoretic pattern of one sample of cyst fluid was obtained and was similar to that of blood and not of cerebrospinal fluid.

Calcification. Plain x-rays showed calcification in 56% of the tumors. In all cases in which calcium was demonstrated radiologically, it was found in the pathological sections. Patients with calcified tumors were more likely to have calcified pineals. In approximately half of the cases in which the pineal was calcified, it was not displaced. There was no increased incidence of calcification in the older age groups. The average preoperative duration of symptoms in those patients having calcified tumors was longer and the postoperative survival shorter than in those with noncalcified tumors.

Patients with large tumor calcification did not show any greater shift of midline struc-
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Pathological Features

The gross tumor characteristics recorded at operation are given in Table 1. There was great variety in the histopathological features. The pathological findings in patients known to have died was correlated with the mean duration of life from the onset of symptoms and the mean duration of postoperative survival. This analysis revealed a slight tendency for patients with marked nuclear pleomorphism to survive for a shorter period than those whose tumors were marked by a uniform "honeycomb" structure (Table 2).

In five patients, histological examination of the tumor was carried out twice. The time intervals between operations were 3 to 6 years. Two cases showed no significant change in the pathological picture. The remaining three showed changes generally associated with increased malignancy, including greater pleomorphism, the presence of giant cells, and more frequent mitoses. Autopsy carried out on two cases after readmission showed residual tumor with diffuse spread through subarachnoid spaces and brain-stem hemorrhages.

Two cases were originally called glioblastoma multiforme on the basis of increased vascularity, endothelial proliferation, pleomorphism, frequent mitoses, areas of necrosis, and palisading. Both, on review, showed areas of homogeneous oligodendrogial cells and some calcifications. One patient survived 5 years, and the other is still alive, without any progression, 17 years postoperatively.

Radiation Therapy

Each of the 63 patients in this series had at least one operative removal; 56% also received radiation therapy at some time during the course of their illness. The decision to treat the patient in this manner was made by the attending neurosurgeon, and no consis-

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**TABLE 1**

Gross tumor characteristics noted at operation in 63 patients

<table>
<thead>
<tr>
<th>Tumor Characteristic</th>
<th>% Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greyish-red, gelatinous</td>
<td>75</td>
</tr>
<tr>
<td>Mushrooming tumor at surface</td>
<td>41</td>
</tr>
<tr>
<td>Gross cyst(s)</td>
<td>34</td>
</tr>
<tr>
<td>Swollen, pale gyri over tumor</td>
<td>17</td>
</tr>
<tr>
<td>Pseudocapsule</td>
<td>10</td>
</tr>
<tr>
<td>Gritty</td>
<td>5</td>
</tr>
<tr>
<td>Dural attachment</td>
<td>3</td>
</tr>
</tbody>
</table>

**TABLE 2**

Analysis of fatal oligodendrogliomas (33 cases)

<table>
<thead>
<tr>
<th>Pathological Characteristics</th>
<th>No. of Cases</th>
<th>Mean Duration Life From Onset Symptoms (yrs)</th>
<th>Mean Duration Post-operative Survival (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marked nuclear pleomorphism</td>
<td>9</td>
<td>8.2</td>
<td>3.9</td>
</tr>
<tr>
<td>Tumor at margins of removal</td>
<td>12</td>
<td>10.6</td>
<td>4.3</td>
</tr>
<tr>
<td>Microcysts</td>
<td>13</td>
<td>10.8</td>
<td>4.3</td>
</tr>
<tr>
<td>Frequent mitoses &gt; 1 / h.p.f.</td>
<td>8</td>
<td>7.9</td>
<td>4.4</td>
</tr>
<tr>
<td>Calcium</td>
<td>17</td>
<td>10.7</td>
<td>4.4</td>
</tr>
<tr>
<td>Marked endothelial proliferation</td>
<td>10</td>
<td>11.3</td>
<td>4.7</td>
</tr>
<tr>
<td>Uniform honeycomb structure</td>
<td>18</td>
<td>12.4</td>
<td>6.1</td>
</tr>
</tbody>
</table>
tent pattern was followed. In recent years it has become more common for patients to receive a course of radiation therapy in the immediate postoperative period.

Of the 33 patients who are known to have died, 64% received radiation therapy. The average total duration of the illness in the radiated group was 12.8 years as contrasted to 11.5 years for those who did not receive radiation therapy. The pre-radiation duration of symptoms in the patients who received it was 8.8 years, while the preoperative duration of symptoms in the patients who were not radiated was 5.1 years. Survival following treatment averaged 4 years for the operated and radiated group and 6.4 years for the operated but not radiated group. An analysis of long- and short-term survivors with and without radiation therapy is given in Table 3. Survival times with repeated therapy show a progressive decrease (Table 4).

Because of the manner in which patients were selected for radiation therapy, our figures do not demonstrate conclusively any benefit in terms of survival. However, it is clear from a study of isolated cases receiving no other therapy except surgical excision that radiation can produce dramatic results in at least some cases of oligodendroglioma. No patient developed cerebral necrosis attributable to the radiation therapy.

Mortality and Survival

The case mortality in this series was 3.2%; the operative mortality 2.7%. The average postoperative survival for all operated cases subsequently known to have died was 5.4 years. The average survival of patients in whom the operating surgeon felt removal had been total was 6.8 years. Average survival where there was marked increased pressure at operation was 4.5 years; where the tumor was known to be vascular at operation postoperative survival was 3.4 years.

It appears in this series that the duration of preoperative symptoms is inversely related to the postoperative survival. Eighty-three percent of the dead patients who had had preoperative symptoms for less than 1 year survived more than 5 years postoperatively, while only 30% of those whose preoperative symptoms had lasted longer than 10 years survived more than 5 years postoperatively (Fig. 1).

Of the 30 patients presumed to be alive, 66% have been able to return to their previous occupation. Only 24% of the 33 patients who are known to have died of their disease had been able to return to work. Five patients who are known to have died had no progression of their symptoms following operation for more than 5 years, but experienced a recurrence and progression of symptoms at intervals of 6 to 19 years after

### Table 3

<table>
<thead>
<tr>
<th>Survival Time</th>
<th>No. Cases</th>
<th>No. Radiated</th>
<th>No. Not Radiated</th>
</tr>
</thead>
<tbody>
<tr>
<td>More than 10 yrs</td>
<td>10</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>2-10 yrs</td>
<td>42</td>
<td>27</td>
<td>15</td>
</tr>
<tr>
<td>Less than 2 yrs</td>
<td>11</td>
<td>2</td>
<td>9</td>
</tr>
</tbody>
</table>

### Table 4

<table>
<thead>
<tr>
<th>Mean Survival</th>
<th>Yrs.</th>
<th>No. Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>After 1st operation</td>
<td>5.4</td>
<td>33</td>
</tr>
<tr>
<td>After 2nd operation</td>
<td>2.1</td>
<td>7</td>
</tr>
<tr>
<td>After 3rd operation</td>
<td>0.3</td>
<td>1</td>
</tr>
<tr>
<td>After 1st radiation</td>
<td>3.9</td>
<td>13</td>
</tr>
<tr>
<td>After 2nd radiation</td>
<td>1.8</td>
<td>4</td>
</tr>
<tr>
<td>After 3rd radiation</td>
<td>0.3</td>
<td>3</td>
</tr>
</tbody>
</table>

**Fig. 1.** Survival curve in 63 patients with oligodendrogliomas.
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treatment. Following recurrence or progression they lived for a further 1 to 4 years. Seven of the patients in the living group have shown no evidence of progression or recurrence of symptoms at 6 to 22 years following treatment.

Eighty-six percent of all the patients in this series have lived longer than 5 years following the onset of their symptoms; 52% have lived longer than 10 years; and 22% longer than 20 years. The relationship of survival to age at onset is given in Table 5.

Discussion

A series of nine cases of oligodendroglioma was described by Bailey and Cushing in 1926 among 254 gliomas. Eight of 210 verified gliomas reported from the Montreal Neurological Institute in 1935 were oligodendrogliomas. In a review of the literature published in 1956, there were 579 cases of oligodendroglia cited in a group of 7,599 brain tumors. There have been a number of other clinical reviews.

The high incidence of seizures, recorded as symptoms on admission in this series, reflects to some extent the fact that many patients were referred to our institute primarily for investigation of this complaint and not as brain tumor suspects. The incidence of this symptom in other series varies between 50% and 78%. Seizures are equally common in cases of oligodendroglia as in cerebral astrocytoma and greater than in glioblastoma.

A high proportion of oligodendroglomas occur in the frontal lobes, 46% to 78% in several large series. We found a relatively low incidence of intraventricular oligodendroglomas; Shenkin, et al., had the highest incidence reported, 24%; other series have ranged between 5% and 10%. An incidence of pathological calcification ranging between 34% and 52% have been reported. The angiographic features of the oligodendroglomas have only rarely been documented adequately.

The great majority of such tumors show up as avascular masses. The brain scan was positive in 6 out of 13 published cases. Our results in 18 cases indicate that the intensity of uptake has no relationship to the prognosis.

McMenemey and Cumings stated that four out of 15 patients with oligodendroglomas had lumbar spinal fluid containing more than 100 mg% of protein. This is at variance with our finding in 30 such cases in which all values were below 70 mg%. There appears to be little data in the literature on the nature of the cystic fluid, but our findings suggest that it is similar to serum and not cerebrospinal fluid.

Gerhardt, et al., carried out LDH-isozyme determinations on five specimens of oligodendrogloma and noted a tendency for the first band to be elevated in four, and bands 2, 3, and 4 to be reduced in all.

The pathological features of these tumors have been adequately described. In our material the vast majority of oligodendrogloma tumor cells, even in well-stained sections, did not become impregnated with silver stains. The fresh smear preparation gave a better demonstration of the cytology of this tumor. Calcium seemed to be laid down progressively in the walls of blood vessels. The granular appearance was frequently an artifact resulting from the cross-sectioning of the remnant of small vessels. We do not consider that any useful function is served by distinguishing between oligodendrogliomas and oligodendroblastomas.

Spread of oligodendroglial tumors via the

| TABLE 5 |
| Relation of survival time to age at onset of symptoms |

<table>
<thead>
<tr>
<th>Age at Onset (yrs)</th>
<th>No. of Cases</th>
<th>% of Total Group (63)</th>
<th>Dead (33) Mean Survival (yrs)</th>
<th>Living (30) Duration of Follow-Up (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>5</td>
<td>8</td>
<td>14.0</td>
<td>21</td>
</tr>
<tr>
<td>11–20</td>
<td>5</td>
<td>8</td>
<td>9.7</td>
<td>6.5</td>
</tr>
<tr>
<td>21–30</td>
<td>16</td>
<td>25</td>
<td>12.8</td>
<td>14.7</td>
</tr>
<tr>
<td>31–40</td>
<td>23</td>
<td>37</td>
<td>13.3</td>
<td>9.1</td>
</tr>
<tr>
<td>41–50</td>
<td>9</td>
<td>14</td>
<td>9.5</td>
<td>11.7</td>
</tr>
<tr>
<td>&gt;50</td>
<td>5</td>
<td>8</td>
<td>4.5</td>
<td>9.7</td>
</tr>
</tbody>
</table>

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cerebrospinal pathways has been emphasized by some authors.\(^4\,5\,25\,38\,40\) In the large series reported by Reymond and Ringertz\(^{11}\) no cases were found that had spread in this manner. This is more in accord with our experience, that while the tumor frequently ruptures through the cortex at a given spot, distant spread via the subarachnoid space or diffuse coating of the subarachnoid space is rare. The high incidence of gross cysts in our series, 34\% (Table 1) is noteworthy.\(^{18}\) Earnest, et al.\(^{13}\) found a 19.4\% incidence of cysts but felt this was an underestimate.

Since all of the cases received surgery and only some were given radiation therapy, we are not able to make any comparison of this method of treatment as opposed to radiation therapy alone. It is also extremely difficult to compare this series with others reported in the literature, because, in many, survival is given only as a mean average after elimination of postoperative deaths, and the living and dead patients are grouped together. It has become our practice to begin radiation therapy within 1 or 2 weeks following operation. We do not feel, as does Shenkin,\(^{25}\) that radiation therapy is best delayed until there is evidence of recurrence postoperatively.

The operative mortality in different series has varied between 4.5\% and 21\%.\(^{7\,19\,28\,31\,36}\) Long postoperative survivals have been noted in several published case reports of oligodendrogliomas.\(^{12\,13\,37}\) The average time postoperatively before evidence of recurrence has varied, but is usually between 1\(\frac{1}{2}\) and 2\(\frac{1}{2}\) years.\(^{8\,20\,31\,32}\)

Of our oligodendroglioma patients, 41\% have survived 5 years postoperatively. This figure compares favorably with that for supratentorial astrocytomas, previously reviewed from this institute, which averaged between 25\% and 37\% depending on the histological subgroup.\(^{29}\) We do not feel that operation shortens the life expectancy of a patient.\(^{14\,15}\) In fact, we believe, as have others,\(^{19\,32}\) that larger removals result in longer survival.

**Summary**

We have reviewed and analyzed 63 cases of oligodendroglioma and have related survival times to therapy, tumor characteristics, and preoperative symptoms.

**Acknowledgments**

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**References**

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