POSTOPERATIVE SURVIVAL OF PATIENTS WITH INTRACRANIAL OLIGODENDROGLIOMA WITH SPECIAL REFERENCE TO RADICAL TUMOR REMOVAL

A STUDY OF 26 PATIENTS

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When Bailey and Hiller suggested in 1924 that certain gliomas were composed of oligodendrocytes, much interest was created concerning the existence of oligodendrogliomas as an entity. In 1926, Bailey and Cushing set apart a group of brain tumors as oligodendrogliomas with histologic verification. Nine cases of such growths out of 254 classified tumors were reported by these authors. One of their patients survived 21 years after the onset of symptoms. Subsequent reports by other authors also suggested that this particular type of glioma was slow in growing and relatively benign. In order to evaluate further the postoperative survival period of patients harboring this tumor, it is our purpose to present the following 26 cases of verified oligodendrogliomas that have been seen at the Lahey Clinic from 1932 to 1949.

Oligodendrogliomas were characterized clinically by Bailey and Cushing as “slow-growing with the appearance of encapsulation, and unless they happen to produce focal and irritative lesions [they] may attain a large size before they make their presence known—so large a size that their removal is well nigh impossible.” Pathologically, “these tumors have a pinkish color on fresh section. They also tend to show calcareous deposits often seen on x-ray films.” According to Cushing, “when fixed, stained and sectioned by ordinary methods the lesions have a characteristic and often unmistakable appearance, the compact mass of small cells with scanty clear cytoplasm having, as Bailey points out, some resemblance to the section of a woody plant.”

In 1935 Elvidge, Penfield and Cone utilized the terms oligodendroglioma and oligodendroblastoma because of differences in the cell types seen in tumors of this group, and Kernohan in 1938 also thought that this differentiation microscopically was desirable.

Although Bailey and Cushing’s earlier observations revealed no mitoses in these tumors, further experience has shown that they are not always as innocent and slow in growth as they were thought to be. Abundant mitoses and metastases have been described by Martin, by Bailey and Bucy and

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by Eisenhardt.\textsuperscript{9} Beck and Russell\textsuperscript{4} reported 4 cases which showed metastases throughout the cerebrospinal pathway. Blumenfeld and Gardner\textsuperscript{5} also reported a case of disseminated oligodendroglioma.

Martin\textsuperscript{14} classified these tumors into (1) oligodendroglioma of the hemispheres and (2) oligodendroglioma of the midline. In 1939 a more detailed classification was made by Löwenberg and Waggoner.\textsuperscript{13} These authors described (1) bilateral oligodendroglioma of the hemispheres, (2) unilateral oligodendroglioma of the hemispheres, (3) intraventricular oligodendrogliomas, (4) oligodendroglioma of the basal ganglions, (5) oligodendroglioma of the brain stem, (6) oligodendroglioma of the cerebellum and (7) oligodendroglioma of the spinal cord. As an example of the latter, Russell and Bucy\textsuperscript{16} recently reported a case in which the initial symptoms were noted 14 years prior to operation.

In respect to the life history and postoperative survival periods of patients having intracranial oligodendroglionas there are significant data from three recent articles, namely, the 25 cases analyzed by Shenkin, Grant and Drew\textsuperscript{17} in 1947, the large series of 165 cases from the Mayo Clinic reported by Earnest, Kernohan and Craig\textsuperscript{8} in 1950 and the series of 74 cases from Olivecrona's clinic reported by Reymond and Ringertz.\textsuperscript{15} Previous to these publications, Bailey and Cushing had reported that 4 of their 9 patients were living 4 years or more following operation, and of the 8 patients of Elvidge, Penfield and Cone, 3 were living, the longest survival being 3 years.

Shenkin, Grant and Drew found that the average survival of their patients was a little less than 2 years, and these authors, as well as Elvidge, Penfield and Cone, thought that the length of postoperative survival was disproportionately shorter than the duration of preoperative symptoms. This feature was not substantiated in the report of Reymond and Ringertz as they found no correlation between length of symptoms and survival after operation.

In the series reported by Earnest, Kernohan and Craig there were 112 patients who left the hospital and from 107 of these some follow-up record was obtained. The average survival period of this group from the time of operation until death or until the patient was last heard from was 48 months, but this figure alone is not of great significance, as the authors pointed out. Many of the living patients had not yet had the opportunity of long survival and thus add to the general average. These authors further clearly showed that a far greater percentage of patients was living after what were termed complete removals than those who had had partial removals or biopsies, so that the eventual survival in the more complete operations would undoubtedly be greater as time went on.

In the series from Olivecrona's clinic the average survival period after operation was 5 years and 3 months, with the longest survival 17\textsuperscript{1/2} years. In this article\textsuperscript{15} there is a complete tabulation of all the cases as to the type of operation and the survival period of each patient. From a study of this table it is apparent that the radical operations accomplished much more than
the nonradical ones, the average survival in the former being just under 7 years, whereas in the latter it was about 3½ years.

In Cushing's series of 2,000 verified brain tumors reported in 1932 there were 27 oligodendrogliomas. Although no statistics of survival were given in this monograph, a further record of these patients was reported by Eisenhardt in 1935. At that time 1 of the patients was still living 9 years following operation, and 5 others had lived from 5 to 13 years.* The vast majority of all these patients were subjected to as complete tumor removals as possible.

PRESENT STUDY

In the present series of 26 patients, there were 17 males as compared to 9 females, with a ratio of a little less than 2 to 1. The age incidence showed an average of 38.9 years with the youngest 15 and the oldest 53 years. The longest probable preoperative duration of symptoms was 12 years in a patient who had recurrent convulsive seizures but since he had also had a cranial injury the etiology of his seizures may be questionable. The average period of preoperative symptoms was 28.6 months, with the shortest 2 months.

Among the preoperative symptoms were seizures in 13 patients (50 per cent) and headaches in 17 (65.4 per cent). Definite papilledema was observed in 14 patients (53.8 per cent). The rest of the symptoms in varying degrees were weakness of extremities, visual disturbance, aphasia, mental retardation, confusion, memory defect, personality change and other pressure symptoms, especially toward the later stages of the disease. Of the 19 patients with intrahemispheric tumors reported by Shenkin et al.,17 12 (63.1 per cent) had epileptic seizures prior to operation. Since none of their 6 patients in the intraventricular group had preoperative seizures it would mean that 48 per cent of their whole group had such attacks, a percentage similar to ours. Our 2 patients with intraventricular tumors were also free from seizures prior to operation. Bailey and Cushing2 called attention to the fact that when people of middle life begin to have epileptiform attacks of obscure etiology, the possible existence of one of these slow-growing lesions must always be borne in mind.

Only 9 of our patients (34.6 per cent) showed calcification in the x-ray films, although a few of the older records had no information with reference to skull films before an air injection had been made.

Twenty (76.9 per cent) of the tumors were hemispheric, 2 (7.7 per cent) intraventricular and 4 (15.4 per cent) cerebellar. Of the cerebral group, 7 (26.9 per cent) were located in the frontal lobe. Five others were in the frontotemporal region. The 4 cerebellar tumors were equally divided as to laterality.

Nine (34.6 per cent) of the 26 patients had more than one operative procedure, with 1 patient surgically treated five times. This patient had

* Two other patients subsequently classified as having oligodendrogliomas were still living and were later operated upon by one of us (G.H.). These patients are, therefore, included in our present series.
been operated on twice previously by Dr. Cushing and survived 45 months. One patient died from a gastric hemorrhage following a second operation after surviving in fairly normal condition for 48 months. Three patients were previously operated upon elsewhere, 2 by Dr. Harvey Cushing and 1 by Dr. Jason Mixter.

Postoperative Survival. Four of our 26 patients died postoperatively, giving a case mortality rate of 15.3 per cent. This figure is for all patients dying in the hospital from whatever cause. Our mortality, therefore, is the same as Cushing's case mortality of 15.4 per cent for oligodendrogliomas as well as that of Olivecrona, 15.3 per cent, but somewhat less than in other reported series which has ranged from 20 to about 25 per cent. Elvidge, Penfield and Cone, however, had no postoperative deaths in their 9 cases in 1935 and Cushing had no deaths among the last 13 patients he operated upon.

Excluding the 4 patients who died in the hospital following operation, there were 22 patients who lived from a few months to many years after their discharge. In some instances our follow-up data are incomplete, but of the 17 from whom we have heard after any length of time, however short, the average duration of life has been 87 months, or just over 7 years. Seven patients have lived from 5 to 10 years, 2 patients have lived 18 years (with 1 still living and well), and 1 patient survived 33 years. In this instance the original operation was performed by Dr. Cushing in 1916 with subsequent operations by the senior author in 1943 and 1946. The patient finally died in 1949.

Six (23.1 per cent) of our 26 patients are still living at the time of this report. Their postoperative survival periods are respectively 216 months, 168 months, 84 months, 76 months, 58 months and 19 months. Two of these patients are retarded mentally to a slight degree. Three have returned to work, although one of these has occasional dreamy states. Our latest patient who had a cerebellar tumor is alive 19 months after operation. He still walks on a wide base and has some residual ataxia of his left extremities. He has also had several seizures, as he did preoperatively.

Six (23.1 per cent) of the tumors revealed foci of astrocytes while the predominant histologic characteristics were those of oligodendroglioma. One other patient, whose verified oligodendroglioma was subtotally removed at the original operation, showed at a subsequent operation almost 2 years later a recurrent tumor with marked histologic changes toward glioblastoma. This patient is still living, but has residual weakness of his right extremities and marked aphasia.

Eight (30.8 per cent) of the cerebral tumors showed cystic areas. In only 2 cases were there definite mitoses with areas showing rapid growth.

DISCUSSION

According to Bucy, oligodendrogliomas form 4 per cent of all gliomas. Our series of 26 similar tumors from a total of 680 gliomas gives a close percentage of 3.8. In Cushing's group of 862 gliomas there were 27 oligodendro-
gliomas or 3.1 per cent, but Olivecrona's percentage (6.7 per cent) is distinctly higher. From a review of the literature several series reports are shown in Table 1, indicating the fairly rare occurrence of this tumor.

In the large series of 165 verified oligodendrogliomas reported from the Mayo Clinic by Earnest, Kernohan and Craig, the authors pointed out, as have most others, that tumors of this type are chiefly cerebral in origin, 151 of their patients having growths above the tentorium and 14 below this structure. They classified the tumors as oligodendrogliomas and oligodendroblastomas according to differences in their microscopic appearance but could not relate this classification to survival periods, nor could any satisfactory system of grading be devised. They estimated the life span of the tumor, from the onset of symptoms until the death of those patients who survived operation and left the hospital, as being somewhere between 8 and 14 years, "and may be much longer."

In the present series, 20 were cerebral, 2 intraventricular, and 4 cerebellar. This is a higher percentage of cerebellar oligodendrogliomas than has been reported in any similar series. In Bailey and Cushing's series of 9 cases, 7 were cerebral and 2 were in the septum pellucidum. Elvidge, Penfield and Cone reported 8 cases, all of which were cerebral. In the series of Shenkin et al.,17 except for the 6 intraventricular tumors, 19 were of the cerebral variety. Greenfield and Robertson11 found 1 oligodendroglioma in the fourth ventricle in a series of 5 cystic oligodendrogliomas. None of the 4 cerebellar tumors in our series was cystic. The patients with cerebellar tumors tended to have a much shorter period of preoperative symptoms, the duration in 3 patients being 2, 3, and 3 months, while in the fourth this period was 36 months. Two of these patients are still alive; the one with the longest period of preoperative symptoms is living a normal and useful life 76 months after operation. The other patient was operated on too recently to evaluate.

Earnest, Kernohan and Craig,8 Löwenberg and Waggoner,13 Shenkin et al.,17 as well as Reymond and Ringertz,15 have shown that cerebral oligo-

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**TABLE 1**

**Frequency of occurrence of oligodendrogliomas**

<table>
<thead>
<tr>
<th>Series</th>
<th>Total Gliomas</th>
<th>Oligodendrogliomas</th>
<th>Percentage of Oligodendrogliomas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cushing (1932)</td>
<td>862</td>
<td>27</td>
<td>3.1</td>
</tr>
<tr>
<td>Greenfield and Robertson (1933)</td>
<td>230</td>
<td>9</td>
<td>3.9</td>
</tr>
<tr>
<td>Elvidge, Penfield and Cone (1935)</td>
<td>407</td>
<td>8</td>
<td>1.7</td>
</tr>
<tr>
<td>Löwenberg and Waggoner (1939)</td>
<td>420</td>
<td>21</td>
<td>5.0</td>
</tr>
<tr>
<td>Reymond and Ringertz [Olivecrona] (1950)</td>
<td>773</td>
<td>52</td>
<td>6.7</td>
</tr>
<tr>
<td>Lahey Clinic (1951)</td>
<td>680</td>
<td>26</td>
<td>3.8</td>
</tr>
</tbody>
</table>

* In the series reported by Shenkin, Grant and Drew,17 and the one by Earnest, Kernohan and Craig,8 the total number of gliomas was not mentioned, so the percentage of oligodendrogliomas is not available.
dendrogliomas have a predisposition to occur in the frontal lobes. These observers also found several tumors with involvement of both frontal lobes. In our series unilateral frontal lobe involvement was present in 7 cases. Five other tumors, however, showed invasion of both frontal and temporal lobes.

Of the intraventricular tumors Shenkin et al.\(^\text{17}\) pointed out that the average preoperative duration of symptoms was \(7\frac{3}{4}\) months with a range of 3 to 11 months. The preoperative period of symptoms in our 2 patients with intraventricular tumor was \(4\frac{1}{2}\) and 12 months respectively, an average of \(8\frac{1}{4}\) months. One of these patients survived only 2 months while the other lived a useful life for 12 years following subtotal extirpation of the neoplasm. It may be pointed out that this patient had only a subtemporal decompression 33 months prior to the second operation when the tumor was attacked directly. The survival period for this patient is, therefore, calculated from the time of the subtotal removal of the tumor.

Postoperative Survival. Our conviction agrees entirely with that expressed by Earnest, Kernohan and Craig that the longest and most satisfactory postoperative periods are obtained by radical tumor extirpation. In the vast majority of our patients an attempt was made to remove all visible tumor tissue, but obviously with this type of growth an absolutely complete excision can never be assured.

We believe that the policy of performing radical, or what may be called grossly total excisions of all gliomas should be emphasized vigorously. There are obvious, but certainly infrequent, exceptions to this policy, for example when to attempt such an operation would leave a patient so crippled that life would be useless. However, even when tumors appear to involve important areas, their removal will often restore function rather than destroy it. Furthermore, it cannot be told with certainty by the gross appearance of a glioma nor by an immediate biopsy the exact nature of the growth or how relatively benign or malignant it may be. At times even glioblastomas will give unexpectedly good results, and certainly with many astrocytomas and the majority of oligodendrogliomas an excellent useful survival may be accomplished. The average of over 7 years in the present series would seem to be conclusive evidence in this respect.

Elvidge, Penfield and Cone\(^\text{10}\) noted that the postoperative survival periods of their 8 cases of oligodendroglioma were disproportionately lower than the preoperative duration of symptoms. Although this was true among some of our patients, the majority showed the reverse order. Perhaps the attempt at a radical total extirpation in every case at the time of the first operation has altered this observation statistically.

**SUMMARY**

Twenty-six cases of histologically verified oligodendrogliomas have been presented with special reference to duration of preoperative symptoms, location of the neoplasms and survival period postoperatively. A comparison
is made with some similar series reports with the purpose of further evaluating the nature of oligodendroglionamos occurring intracranially.

Although some of the tumors showed mitotic figures histologically, they were relatively few. Only one showed abundant mitoses. These occurred in a recurrent tumor 2 years after the original operation. It may be concluded that although oligodendroglionamos occasionally grow wild, as they have been observed to do by other investigators, they are in the main slow growing so that every effort should be made to remove them as completely as possible when encountered.

Longer survival periods after radical tumor extirpation are evident from the study of previously reported cases, and this policy is likewise substantiated in the present series by an average postoperative survival period of over 7 years.

REFERENCES