Control of temporal lobe epilepsy following en bloc resection of low-grade tumors


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 Thirty-one patients with a mean age of 18.9 years (range 3 to 53 years) who underwent temporal lobe surgery for tumor-related epilepsy over a 14-year period are presented. All had suffered chronic drug-resistant temporal lobe seizures (mean age at onset 6.9 years, range 0 to 30 years; mean duration of condition 11.9 years, range 3 to 39 years). Preoperative interictal scalp electroencephalography tracings indicated unilateral localized epileptic foci in 90% of patients, and computerized tomography scans showed abnormalities within the temporal lobe in 87%. All patients underwent en bloc temporal lobectomy. No patient received adjuvant radiotherapy or chemotherapy. Review of the histological material showed dyssembryoplastic neuroepithelial tumor in 27 (87%) of the specimens and microscopic evidence of incomplete removal of tumor in 22 (71%). At long-term follow-up evaluation (mean duration 5.8 years, range 1 to 14 years), 81% of patients were completely free of seizures (Engel grade I) and 10% were almost seizure free (Engel grade II) with no deaths reported in either early or late follow-up review. Only one patient in the series failed to benefit from the surgery. Four patients suffered permanent neurological deficit causing a mild disability. Psychological assessment showed no significant fall in verbal or performance intelligent quotient for the group, but a mild memory impairment was evident in 32%. Behavioral and social aspects improved in nearly all (94%) cases. Relief of seizures could not be predicted by intraoperative electrocorticography, and outcome was independent of the completeness of tumor resection. Postoperative electroencephalographic findings identified epileptiform potentials in 65% of patients, which were associated with a worse seizure-control outcome grade.

KEY WORDS • temporal lobe epilepsy • seizure • temporal lobectomy • dyssembryoplastic neuroepithelial tumor • computerized tomography • magnetic resonance imaging

LOW-GRADe Tumors are found in 10% to 20% of surgical specimens resected for chronic temporal lobe epilepsy. The majority of these are indolent neoplasms as indicated by the chronicity of the epilepsy, absence of neurological focal deficit, long-term survival, and benign pathological features. In 1958, Cavanagh wrote about such tumors from operative specimens resected by the late Murray Falconer. Further instances have been encountered at the Maudsley Hospital. In the past they have been described by a variety of terms that were related to the appearance of the individual lesions. These terms reflected doubts about their origin, namely, whether these entities were malformation, hamartoma, or indolent low-grade astrocytoma or oligodendrogloma. More recently, it has become evident that many of these lesions are similar to those termed "dyssembryoplastic neuroepithelial tumor" by Daumas-Duport, et al., and the term is currently used for such cases.

Computer-assisted radiographic imaging allows the noninvasive diagnosis and accurate localization of many temporal lesions and provides the opportunity to plan the extent of resection preoperatively. The prognosis for seizure control following temporal lobe surgery is generally more favorable for tumor-related epilepsy than for non-neoplastic conditions such as mesial temporal sclerosis. Furthermore, seizure control can be achieved without total removal of the lesion. It is therefore possible that precise surgical removal of such tumors, guided by advanced imaging analysis and intraoperative electrocorticography (ECoG), may not be necessary for this subgroup of epilepsy patients.

We present a retrospective study of patients who have undergone a simple 5- to 6-cm en bloc temporal
lobectomy for tumor-related epilepsy. Our findings suggest that complete or near-complete seizure control can be safely achieved in most cases by standard resection.

**Clinical Material and Methods**

**Patient Selection**

Among 180 patients undergoing temporal lobe resection for chronic epilepsy in the Neurosurgical Unit at the Maudsley Hospital between 1976 and 1990, 31 (17.2%) had tumor-like lesions in the resected specimen. The case notes and outpatient correspondence of these 31 patients have been reviewed. All had suffered chronic drug-resistant epilepsy (mean duration 11.9 years, range 3 to 39 years) with a mean age at onset of 6.9 years (range 0 to 30 years). No predisposing factors (such as febrile convulsions) were identified for any patient, and all were judged to be without clinical evidence of raised intracranial pressure or focal neurological deficit. The age at operation ranged between 3 and 53 years (mean 18.9 years).

**Preoperative Investigations**

The preoperative investigations consisted primarily of electroencephalography (EEG) recordings, computerized tomography (CT) scanning, and psychometry. Less frequently used techniques included air encephalography in the earliest four cases, cerebral angiography in two, carotid amobarbital (Amytal) testing in nine, and magnetic resonance (MR) imaging in one.

**Electroencephalography Studies.** Interictal scalp recordings were abnormal in all cases, and lateralizing in 28 (90%). The three patients with inconclusive interictal recordings proceeded to scalp telemetry, which demonstrated the unilateral onset of seizure activity during an ictus. The combined scalp EEG and telemetry investigations indicated left-sided lateralization in 18 (58%) cases and right-sided lateralization in 13 (42%).

**Computerized Tomography Studies.** Conventional orientation and reverse-axial contrast CT scans (Fig. 1) were obtained in all but one patient. Abnormalities were seen in 27 scans (87%) and consisted of areas of calcification often associated with an adjacent region of low density in 14 (52%), an area of low density alone in 10 (37%), and the only detected abnormality (dilation of the temporal horn) in three (11%). The location of any abnormality was accurately identified on the reverse-axial images (Fig. 1 center and right). The side of the abnormality visualized on CT corresponded to EEG lateralization in all cases.

**Neuropsychological Evaluation.** Preoperative psychometric assessment was carried out in 26 patients (84%). The Wechsler verbal intelligence quotient (VIQ) and performance intelligence quotient (PIQ) were obtained, and verbal and spatial memory were assessed using a battery of investigations including the Wechsler Logical Memory Subtest and the Benton and the Rey Osterreith tests. Any disturbance in behavior was noted, and the effect on social behavior was documented for each individual. An intracarotid sodium Amytal (Wada) test was carried out in nine cases to determine cerebral speech dominance, which was left-sided in all, and to identify patients who might sustain an amnesic syndrome following the operation. However, the Wada test did not lead to exclusion from surgery or result in altering the extent of resection for any patient.

**Surgical Procedures.** Eighteen patients underwent a left-sided and 13 a right-sided 5- to 6-cm en bloc temporal lobectomy. The posterior segment of the superior temporal gyrus was spared on left-sided resections. Pre- and postresection ECoG were recorded in all but one patient. These recordings were not used to direct the extent of resection.

**Pathological Analysis.** The histological material from all cases was reviewed by one of us (M.H.). The extent of tumor removal was examined, and the hippocampus was also reviewed for evidence of mesial temporal sclerosis.

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![Fig. 1](https://example.com/fig1.png)

**Fig. 1.** Computerized tomography scans of a patient with chronic epilepsy associated with a calcified lesion in the left temporal lobe. Left: Conventional scan oriented parallel to the orbitomeatal line. Center: Scout image showing the orientation adopted for fine-slice (3-mm) reverse-axial scans. Right: Reverse axial image of the temporal lobe showing the position of the calcified lesion lateral to the temporal horn.
TABLE 1

Seizure control outcome classification of Engel

<table>
<thead>
<tr>
<th>Grade</th>
<th>Seizure Control</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>seizure free except for an occasional aura</td>
</tr>
<tr>
<td>II</td>
<td>rare seizures (&quot;almost seizure free&quot;); 1–2 seizures per year</td>
</tr>
<tr>
<td>III</td>
<td>worthwhile reduction in the frequency and/or severity of seizures</td>
</tr>
<tr>
<td>IV</td>
<td>no worthwhile improvement</td>
</tr>
</tbody>
</table>

Postoperative Investigations, Treatment, and Follow-Up Study. Three months postoperatively, scalp EEG recordings were obtained in 26 cases (84%) and repeat psychometric assessment was performed in 21 (68%). Patients were reviewed at regular 3-month intervals for the first 2 years and annually thereafter. A few patients had repeat EEG and psychometric investigations at the end of the first postoperative year, but the results of these did not differ significantly from those obtained at 3 months. For 2 years postoperatively, all patients received the full doses of anticonvulsant drugs as given preoperatively; slow drug withdrawal was then offered if they were completely seizure free. Patients who continued to experience seizures were maintained on preoperative doses of anticonvulsant drugs. No patient received adjuvant radiotherapy or chemotherapy.

Postoperative seizure control was graded according to a simplified version of Engel’s classification11 (Table 1), and changes in the behavioral and/or social aspects for individual patients were analyzed. The mean follow-up period for the series was 5.8 years (range 1 to 14 years), and more than one-half of the patients have been seen regularly for over 5 years (Fig. 2).

Results

Postoperative Mortality and Morbidity Findings

No patient died as a result of surgery, either in early or late follow-up review. Early morbidity occurred in 12 patients (39%) and usually consisted of a transient neurological deficit. There was one case of postoperative staphyl_occocal meningitis. Permanent neurological deficit caused mild disabilities in four patients (13%), and chronic osteomyelitis requiring cranioplasty occurred in four others (Table 2).

TABLE 2

Postoperative neurological morbidity in 31 patients

<table>
<thead>
<tr>
<th>Neurological Deficit</th>
<th>Temporary</th>
<th>Permanent</th>
</tr>
</thead>
<tbody>
<tr>
<td>hemiparesis</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>dysphasia</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>third nerve palsy</td>
<td>3</td>
<td>—</td>
</tr>
<tr>
<td>homonymous hemianopia*</td>
<td>—</td>
<td>2</td>
</tr>
<tr>
<td>total</td>
<td>12</td>
<td>4</td>
</tr>
</tbody>
</table>

* All other patients had an upper quadrant field deficit.

TABLE 3

Pathological diagnosis of resected specimens in 31 patients

<table>
<thead>
<tr>
<th>Pathological Diagnosis</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>dysembryoplastic neuroepithelial tumor</td>
<td>27</td>
</tr>
<tr>
<td>ganglioglioma</td>
<td>3</td>
</tr>
<tr>
<td>hamartoma</td>
<td>1</td>
</tr>
</tbody>
</table>

Pathological Examination

On review of the histological material, the majority of these lesions (87%) could be classified as dysembryoplastic neuroepithelial tumor (Table 3). The previous diagnoses commonly included malformation, hamartoma, low-grade astrocytoma, astro-oligodendroglioma, or oligodendroglioma. The tumor extended up to the resection margins in 22 (71%) of the specimens indicating microscopically incomplete removal in these patients. Seizure control outcome was independent of both tumor pathology and completeness of resection. The hippocampus was without tumor involvement and sufficiently preserved for histological evaluation in 26 specimens. Examination of these specimens showed that five had definite histological features of mesial temporal sclerosis.

Seizure Control

At last follow-up review, 25 patients (81%) had achieved a grade I outcome as classified by Engel, and three patients (10%) had achieved a grade II outcome (Fig. 3 left). A further two patients (6%) reported worth-

![Fig. 2. Bar graph showing the postoperative follow-up period for the series.](image)

![Fig. 3. Bar graphs showing postoperative seizure control according to Engel’s classification11 (see Table 1). Left: Seizure outcome of the entire series. Right: Seizure control in relation to age at operation. Patients receiving surgery after the age of 15 years had a slightly worse prognosis (shaded bars) than those operated on at or below this age (solid bars); however, the difference between these groups failed to reach statistical significance.](image)
while reduction in the frequency and/or severity of their seizures (grade III), and only one patient (3%) did not benefit from surgery (grade IV). There were no patients with late recurrence of epilepsy, and those who did experience postoperative seizures did so within 1 year of operation. Of the five patients with dual temporal pathology (dysembryoplastic neuroepithelial tumor and mesial temporal sclerosis), four achieved postoperative seizure control outcome of grade I and one achieved a grade III outcome. Of the 25 patients who are seizure free, 13 no longer receive medication, six are reducing their course of anticonvulsant drugs, and six have chosen to continue medication to prevent revoking of their driver’s license or are due to begin drug withdrawal.

Patients operated on at or before the age of 15 years appeared to have a marginally better outcome than those undergoing surgery at a more advanced age (Fig. 3 right). Grade I outcome was achieved in 88% of the younger group compared to 60% of the older group. However, this difference failed to reach statistical significance.

**Electroencephalography Findings**

Electroencephalography tracings were graded as either type A (no epileptiform potentials), type B (occasional epileptiform potentials), or type C (frequent epileptiform potentials). Preoperative ECoG indicated a high percentage of type C traces (90%) with the remainder being type B (Fig. 4 left). Postoperative recordings showed a general improvement with fewer type C traces (29%), more type B (55%), and a few type A (16%) (Fig. 4 left). However, an improvement from the pre- to postoperative ECoG tracings did not predict a better outcome of seizure control compared to those who did not show an improvement (Fig. 4 right).

**Postoperative Scalp Electroencephalography**

Repeat scalp EEG tracings 3 months postoperatively indicated abnormal recordings in 17 patients (65%), with unilateral focal epileptogenic foci over the operative site in 12 (46%) and a more diffuse bilateral abnormality in five (19%). Patients in whom the postoperative EEG was abnormal had a significantly worse seizure control outcome (p < 0.01, chi-squared test) than those with normal recordings (Fig. 5).

**Psychometric Assessment**

Postoperative VIQ and PIQ scores showed no significant change from the preoperative values for the group. The mean preoperative VIQ score (Fig. 6 left) was 90.0, with a 95% confidence interval (CI) of 79 to 100; the postoperative mean score was 86.8 with a 95% CI of 79 to 94.2. The mean PIQ score (Fig. 6 right) was 97.2 preoperatively (95% CI 90.7 to 104) and 98 postoperatively (95% CI 91.4 to 106). Regression analysis detected no correlation between postoperative psychometric scores and the patient’s age, sex, or duration of the condition.

**Effects of Surgery on Memory, Behavior, and Social Expression**

Mild impairment in memory was detected in seven (33%) of the 21 patients tested postoperatively relative to their preoperative scores. Six patients displayed an impaired verbal memory, two following a left-sided and four a right-sided lobectomy. One patient suffered a spatial memory deficit after a left-sided lobectomy. Despite this, analysis of the behavioral and social aspects for individual patients indicated distinct improvement in 29 cases (94%). Deterioration occurred in only two patients, both of whom continued a downward preoperative course without the operation appearing to alter this trend significantly.

**Discussion**

The data presented indicate that chronic temporal lobe epilepsy related to a low-grade tumor can be safely treated by en bloc temporal lobectomy with minimum associated morbidity. Seizure control was favorable...
Temporal lobe epilepsy following en bloc resection

Fig. 6. Bar graphs showing the Wechsler verbal intelligence quotient (VIQ) (left) and the performance intelligence quotient (PIQ) scores (right) in 21 patients before (solid bar) and after (hatched bar) surgery. No significant difference was identified. Numbers in parentheses indicate the 95% confidence limits.

when compared to other series. Higher cognitive function was not significantly impaired, and in nearly all patients there was an improvement in the behavioral and social effects of their condition.

Preoperative Investigations

It would seem that this subgroup of patients with temporal lobe epilepsy related to low-grade tumor can proceed to surgery with limited preoperative evaluation. A CT scan is required to detect abnormalities indicative of a low-grade, non-space-occupying tumor. The use of reverse-axial images to enhance CT abnormalities within the temporal lobe is recommended, particularly for the detection of low-density regions. As a result, 87% of patients undergoing scans in this series demonstrated abnormalities suggestive of tumor. Magnetic resonance imaging was limited to one case in this study that showed no abnormality. However, our more recent experience suggests that MR imaging is more sensitive for noncalcified lesions, as reported by others.

The second requirement is an interictal scalp EEG recording that shows epileptiform phenomena lateralizing to the same side as the tumor. This was achieved without the use of scalp telemetry for ictal recordings in all but three patients. Other more invasive localizing electrophysiological methods, such as recording from foramen ovale and depth electrodes, were not necessary although they are frequently needed during the investigation of epilepsy in our unit. There are reports of successful outcome after resection of an intracranial lesion despite lateralization of epileptogenic foci to distant ipsilateral or even contralateral regions. This evidence questions the need for any electrophysiological investigation in epileptic patients who have a preoperatively identified structural abnormality.

Intraoperative Investigations

Surgical resection was standard for all patients. Intraoperative ECoG recordings did not influence the extent of cortical resection, and we could not use them to predict the seizure control outcome. A total of 26 patients displayed temporal lobe abnormality on CT scanning together with a corresponding interictal EEG focus. Thus, in retrospect, approximately 84% of the present group of epilepsy patients could have proceeded to temporal lobectomy without further investigation. The achievement of seizure control by operative resection of the structural lesion rather than the epileptogenic focus has also been demonstrated by Awad, et al. Furthermore, postoperative scalp EEG recordings did not contribute to the management of these patients, although they were of some predictive value. All patients with normal postoperative recordings achieved a grade I seizure control outcome; however, an abnormal postoperative EEG was not necessarily associated with a poor outcome. These findings parallel in many ways the recent experiences of Boon and colleagues in their assessment of intractable partial seizures associated with intracranial lesions.

Effects of Surgery on Cognitive Function

The results of the pre- and postoperative neuropsychological analyses indicated no significant drop in VIQ and PIQ scores. A mild degree of memory impairment was detected in 33% of patients, which was independent of the side of resection, and there appeared to be no social consequence of this. Only a small variation in intelligence quotients has been reported following anterior temporal lobectomy for nontumor-related chronic epilepsy in adults and children, and the improvement in behavioral and social effects was expected.

Tumor Pathology

Eighty-seven percent of our specimens were classified as dysembryoplastic neuroepithelial tumor. Our series does not include any patients with conventional astrocytomas or oligodendrogliomas. The term dysembryoplastic neuroepithelial tumor was coined by Daumas-Dupont and colleagues, and has recently been included in the World Health Organization classification for brain tumors. Although often situated in the temporal lobe, dysembryoplastic neuroepithelial tumors have been found in other areas of the cerebral mantle, such as the parietal and frontal regions. The lesion can be diffuse and ill defined and may contain cysts, but more commonly it consists of multiple nodules widely dispersed within the specimen. The leptomeninges, cortex, and white matter may be involved. Microscopically,
dysplastic neuroepithelial tumor has a heterogeneious appearance with groups containing numerous small cells with rounded nuclei and little cytoplasm, mature neurons, and varying numbers of astrocytes. The small round cells were originally thought to be oligodendrocytes, but electron microscopic examination of the cells has indicated neuronal differentiation in several cases. This evidence adds weight to the theory that the lesion arises from nests of primitive neurons that have been arrested in their embryonal migration. The lesions appear to be indolent, and no adjuvant postoperative therapy is indicated. Other low-grade glial tumors also appear to follow a benign course. Hence, despite incomplete tumor removal in 71% of the patients in this series, no clinical recurrence has been noted.

Conclusions

This study serves to reinforce the identity of a subgroup of patients suffering from chronic epilepsy associated with low-grade tumors in the temporal lobe. The majority of these lesions can be identified in such patients by high-resolution CT scans and the laterality of the epileptogenic focus usually confirmed with simple interictal EEG recordings. The tumors are invariably indolent with no tendency to progress. Therefore, in bloc temporal lobe resection with preservation of the dominant superior temporal gyrus can be safely undertaken without further neuropsychological evaluation as there appears to be no significant risk of intellectual handicap. Adjuvant therapy does not appear necessary.

References

Temporal lobe epilepsy following en bloc resection


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