Resection strategies in tumoral epilepsy: Is a lesionectomy enough?

Nitin Tandon and Yoshua Esquenazi

Vivian L. Smith Department of Neurosurgery, Medical School, University of Texas Health Science Center at Houston, Houston, Texas, U.S.A

SUMMARY

Resection strategies in patients with tumor-related epilepsy vary from lesionectomy to larger epilepsy operations with no consensus on optimal approaches. The objective of this study is to use our prior experience in the management of these patients, to derive optimal strategies for the surgical management of epilepsy related to brain tumors. A prospectively compiled database of epilepsy and tumor patients was used to identify patients who underwent surgical resection of a neoplasm but then developed epilepsy, or who presented with epilepsy and were found to harbor a brain tumor. Seizure frequency, histopathology, type of surgical resection, and outcomes were compiled. Of 235 epilepsy surgery patients and 75 low/intermediate grade glioma surgery patients, 13 (5.5%) and 21 (28%) patients, respectively, had tumoral epilepsy. Twenty-two patients were male and 18 tumors were in the left hemisphere. Tumoral epilepsy occurred predominantly in temporal (50%) and perirolandic (26.5%) locations. The etiology was WHO grade I tumors in 29%, grade II in 35%, and grade III in 33%. In the epilepsy group, following lesionectomy in three and tailored resections in the majority, seizure outcomes were Engel class I in all except one case. In the tumor group, after the initial operation seven additional resections were performed due to seizure recurrence. Outcomes in this group were Engel class 1A in 18 patients and 1B, 1C and 1IA in 1 patient each.

Drawing upon these data, we propose a classification of the likely reasons of failure in seizure control in patients with tumoral epilepsy. This review reiterates the concept that a complete resection of the lesion is the best approach for dealing with tumors presenting with epilepsy. Overall excellent outcomes can be accomplished following aggressive initial tumor resection, re-resection in the context of recurrence, and epilepsy style operations in selected patients with a longer history of seizures.

KEY WORDS: Lesionectomy, Temporal lobectomy, Epilepsy, Low-grade tumors.

Seizures are the most frequent presenting symptom in patients with low-grade brain neoplasms and are more prevalent when the lesion is located in or around the temporal lobe (Chang et al., 2008; Fried et al., 1994). Improvements in imaging techniques in the evaluation of patients with seizures have improved detection of these lesions (Bergen et al., 1989). The most common intrinsic tumors that lead to seizure disorders include low-grade astrocytomas, oligodendrogliomas, and gangliogliomas (Berger et al., 1993; Clusmann et al., 2002; Lombardi et al., 1997). Traditionally, brain tumors associated with epilepsy have been managed by neurooncologic surgical principles with cytoreduction as the main goal. Unfortunately, resection of the epileptogenic zone, which may be at the margins of the tumor or distant from the tumor, is not a goal of this strategy (Gilmore et al., 1994). Given the long life expectancies that patients with low grade tumors can often expect, it is crucial to also address the epilepsy, so as not to adversely affect the quality of life in these patients (Klein et al., 2003). The optimal surgical strategies in patients with tumoral-epilepsy, particularly as related to lesions in the temporal lobe, remain poorly defined. Recent work shows that the extent of resection significantly predicts seizure freedom following surgery, with tailored resections achieving higher rates of seizure freedom than gross total or subtotal resections (Englot et al., 2012). In this review, we present our experience in managing patients presenting with medically refractory...
tumoral epilepsy and use this to generate a classification scheme for failure following surgery in tumor-related epilepsy.

**METHODS**

Two separate prospectively compiled patient databases of all consecutive patients undergoing surgery over an 8-year period (2005–2012) at our institute were used. One comprised all patients who underwent cranial epilepsy procedures (n = 235), and the other included all patients who underwent resection of low or intermediate grade brain tumors (n = 75). Demographic data, seizure frequency, tumor histology, type of surgical resection, tumor location, radiographic findings, and outcomes were compiled. The local institutional Committee for Protection of Human Subjects approved the compilation of data.

**RESULTS**

The total study population included 34 patients ranging in age from 4 to 55 (mean 33 years). The first group of patients included 13 patients (5.5%) with epilepsy related to a neoplasm identified from a cranial epilepsy database of 235 patients. The second group included 21 individuals (28%) with tumoral epilepsy and were identified from a low/intermediate grade glioma database of 75 patients. Time to diagnosis from seizure onset was 4 years (median) in the first group and 1 week in the second group. Histopathologic diagnosis was as follows: WHO grade I tumors (Louis et al., 2007) (dysembryoplastic neuroepithelial tumors [DNTEs], gangliogliomas, pilocytic astrocytoma, and angiocentric gliomas) in 29%, grade II (oligoastrocytoma, diffuse astrocytoma, oligodendroglioma, and ependymoma) in 41%, and grade III (anaplastic astrocytoma, ependymomas, and oligoastrocytoma) in 26%. One pediatric epilepsy patient was diagnosed with a primitive neuroectodermal tumor (PNET), WHO grade IV. Twenty-two patients were male and 18 tumors were located in the left hemisphere. The most common locations were in the temporal lobe in 17 (50%)—9 were in lateral, and 5 in mesial (amygdala-hippocampus) temporal structures, and 3 extended into insular cortex. Tumors were in perirhinal in 9 (26.5%), supplementary motor area (SMA) in 5, and lateral cortices in 4. Other locations (frontal, parietal, occipital) were found in 23.5% of the cases. In the epilepsy group, maximal lesionectomy was accomplished in nine patients; and electrocorticography (ECoG) was used in six of these to tailor the resection. In addition to lesionectomy, three patients underwent an anterior temporal lobectomy and amygdalo-hippocampectomy (ATL+AH). In these cases, tumors were located in the amygdala (one) and para-hippocampal gyrus (two). Subdural electrodes (SDEs) as part of a phase II evaluation were utilized in two patients prior to the resection, followed by a tailored lesionectomy. Seizure outcomes in this group were Engel class I in all (IA, 10; IB, 2) except for one (class III) patient. In the tumor group, maximal lesionectomy was performed in all patients, including resection of the amygdala and hippocampus in three cases due to neoplastic involvement of these mesial structures. Seven additional resections (between 1 and 4 years) were performed after seizure recurrence in this group—all related to residual or recurrent tumor after initial surgery. Eventual outcomes in this group were IA, 18; IB, 1; IC, 1; and IIA, 1. Table 1 demonstrates the distribution of cases according to the proposed classification scheme for failures following surgery in these patients.

**DISCUSSION**

Although seizures are a common presenting symptom of brain tumors, patients with medically refractory epilepsy may be found to harbor a tumor. On account of the indolent course and long survival times that can be achieved with early and effective management of low-grade tumors, seizure control in these patients is imperative. Surgical strategies in tumor-related epilepsy remain controversial, and vary from lesionectomy only, to more extensive resections (Berger et al., 1993; Kirkpatrick et al., 1993; Lombardi et al., 1997), particularly in tumors located in or around the temporal lobe. Factors that need to be considered prior to surgery include tumor location (eloquent vs. noneloquent cortex), epileptogenic zone beyond the tumor (hippocampus and/or amygdala), scar produced after a prior lesionectomy (which can be epileptogenic), residual tumor, laterality, preserved cognitive functions around the lesion, and seizure recurrence in the setting of tumor regrowth. In this review, we present our experience and the management strategies employed in decision-making for patients with tumoral-epilepsy.

Similar to the observation in other series, the most common tumors in our group included low-grade gliomas and GNTs (glioneuronal tumors) (Table 2). Of interest, the time interval between seizure onset and surgery differed markedly between these groups. In the first group of patients, this interval lasted 4 years (median). Most of the tumors in these patients included grade I and II tumors, with the exception of one pediatric patient who harbored a PNET, who was diagnosed 4 months after seizure onset. In the second group of patients, higher-grade tumors were found, with a predominance of grade III tumors (anaplastic astrocytoma) in 47% of the cases, and seizures in this population began a median of 2 weeks prior to resection. The shorter time to surgery after seizure onset in this group is likely related to the more aggressive oncologic nature of lesions, and the concern in all caregivers about progression of the tumor without prompt intervention. The location of tumors is an important contributing factor of tumor-related epilepsy, and seizures are commonly
seen in tumors that are situated predominantly in the frontal, temporal, and insular region as well as those that are located close to the cortical surface (Chang et al., 2008). In our group, the majority of tumors (50%) were in the temporal and in the perirolandic (26.5%) regions, in keeping with the greater epileptogenic potential of these brain regions. The pathophysiologic mechanisms of tumor-related epilepsy (discussed earlier in this supplement) include focal disruption of the blood–brain barrier (BBB), metabolic imbalances related to enzymatic dysregulation around the tumor, and alterations in tissue water content (Ivens et al., 2007; Rajneesh & Binder, 2009).

Patients presenting with epilepsy who are found to harbor a brain tumor are optimally managed, keeping both oncologic and epilepsy principles at the forefront. Tumor resection needs to be maximized and thoughtful consideration given to a “lesionectomy-plus” approach in patients with tumors involving mesial temporal structures. The presence of subtle signal changes or abnormal electrical activity in the hippocampus should be looked for specifically (Lombardi et al., 1997). In the setting of tumoral-epilepsy, the presence of dual pathology (gliosis, cortical dysplasia, and hippocampal sclerosis) may be responsible for persistent seizure activity following tumor removal (Englot et al., 2012). Decisions about the extent of the resection will eventually depend on the lateralization and localization of language and memory functions, and need to be individualized in the context of each patient’s neuropsychological profile and functional state.

Patients who develop seizures following a resection need to be carefully evaluated and re-imaged, with a high suspicion for tumor recurrence (Chang et al., 2008). In these circumstances, the recurrence can be treated as a focal epileptogenic lesion, unless extension into the mesial temporal structures has occurred.

Satisfactory seizure outcomes as seen in this and other series can be achieved in patients with tumor-related epilepsy (Duffau et al., 2002; Zaatreh et al., 2003). In these patients, the goal should be to localize the epileptogenic zone, which may be distant from the tumor itself, and invasive intracranial recordings or intraoperative ECoG are helpful in tailoring the resection. The favorable seizure outcomes seen in this series are likely related to the aggressive initial tumor resection in the first group, as well as an early re-resection strategy in the context of tumor recurrence in the second group. Three patients in the first group had a prior lesionectomy and presented to our institution with persistent seizures. Further imaging studies revealed evidence of residual tumor in two of them. With targeted re-resections in two (invasive intracranial recordings with postresection ECoG in one, and an awake craniotomy in
another one) as well as resection of the mesial structures in one (temporal lobe tumor), Engel class I outcomes were achieved in all three patients.

We propose a tumoral epilepsy treatment outcomes classification as detailed in Table 1. Given the variables inherent in these outcomes, it is important that there is an evidence base and sufficiently powered statistical rigor to decision making in the treatment of our patients. Stratification of outcomes and future multivariate study is likely to significantly empower this.

**CASE ILLUSTRATIONS**

**Case 1**

A 47-year-old right-handed man presented with a recent history (3 weeks) of new-onset seizures. He was evaluated with a magnetic resonance imaging (MRI) scan (Fig. 1) and was found to have a right frontal lesion in the posterior frontal lobe adjacent to primary motor cortex. Preoperative functional MRI (fMRI) and diffusion tensor imaging (DTI) were used to localize the motor cortex and the...
Figure 2.
(A) Preresection and (B) postresection photographs of right perirolandic cortex with labeled sites for primary motor and sensory cortices (H, hand; T, tongue; F, face; J, jaw); the blue string demonstrates the orientation of the central sulcus, and coincided with the site of maximal phase reversal of cortical somatosensory evoked potentials.

Figure 3.
(A) Preoperative axial T2-weighted MRI of the brain demonstrating diffuse hyperintense signal changes in the insular region, and frontal and temporal lobe, involving the operculum. (B) Postoperative T2-weighted MRI shows complete resection of a diffuse astrocytoma. A temporal lobectomy and amygdalohippocampectomy was also performed.
corticospinal tract. He underwent an awake craniotomy with motor mapping, and a subtotal resection of a diffuse astrocytoma was achieved (Fig. 2). Following surgery, his focal motor seizures subsided and he was managed conservatively with follow-up imaging studies. He remained on one seizure medication throughout this time. Three years later his seizures recurred and imaging studies showed disease progression. He underwent re-resection via awake craniotomy with motor mapping, and he subsequently received adjuvant chemotherapy and radiation therapy. He has remained seizure free (Engel class I) for more than 1 year on one seizure medication.

Case 2

This 63-year-old right-handed male rancher presented with 6-month history of left arm tingling and numbness. These episodes lasted for about 30 min and subsided spontaneously with a frequency of once per week. Initially the patient was referred to a cardiologist and was diagnosed with a variant angina. He underwent cardiac catheterization and stent placement with no improvement. His events increased in frequency, which were now accompanied by transient confusion. He eventually developed a grand mal seizure that led to an MRI scan of the brain (Fig. 3). The patient underwent a right craniotomy and gross total resection of the lesion including a temporal lobectomy and amygdalohippocampectomy, as well as resection of the insular component (Fig. 4). Following surgery he became seizure-free (Engel class I).

Figure 4.
Intraoperative photograph demonstrating the resection cavity following the resection. The sylvian vein and middle cerebral artery branches are skeletonized to maximize resection of the insula and frontal operculum. An anteromesial temporal lobectomy has also been performed.

Epilepsia © ILAE

Conclusion

Patients with tumor-related epilepsy are frequently found to have low-grade tumors. Both tumor control and seizure freedom can be achieved with high frequency in this population. The epileptogenic zones may be distant from the lesion, and a tailored resection based on the results of presurgical evaluation and anatomical-electroclinical correlations including intraoperative ECoG needs to be considered. The goal in these patients is to achieve not only oncologic success but also to optimize chances of seizure-free outcomes. We used an aggressive surgical intervention targeting the lesion except where medial temporal structures were involved, where a typical temporal lobectomy was performed. The excellent outcomes seen in this group (Engel class I in 94%) relate to aggressive initial tumor resection and early re-resection in the context of recurrence.

Disclosures

The authors have no conflict of interest in relation to this work. We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

References


