Surgical strategies and seizure control in pediatric patients with dysembryoplastic neuroepithelial tumors: a single-institution experience

KRASIMIR MINKIN, M.D.,1 OLIVIER KLEIN, M.D.,1 JOSETTE MANCINI, M.D.,2 AND GABRIELlena, M.D.1

Departments of 1Pediatric Neurosurgery and 2Pediatric Neurology, University Hospital La Timone, Marseille, France

Object. Dysembryoplastic neuroepithelial tumors (DNTs) are commonly associated with medically resistant epilepsy that usually starts in childhood. Presurgical workup and surgical strategies remain controversial. The authors present a study of long-term seizure outcome after noninvasive presurgical investigations and different surgical strategies were used in a series of pediatric patients.

Methods. Twenty-four children who underwent operations at a single center between 1986 and 2006 were eligible for this retrospective study. The authors reviewed medical records including sex, age at seizure onset, age at surgery, seizure type and pharmacoresistance, lesion location, extent and complications of resection, histopathological findings, prescription of seizure and antiepileptic drugs, outcome, and tumor recurrence.

Results. At the last follow-up examination (range 1–16 years after initial treatment, mean 6.7 years) 20 children (83.3%) were seizure free. The authors did not find the rundown phenomenon in any of the patients. Complete antiepileptic drug withdrawal was achieved in 12 children (50%). In 4 of 15 children with temporal DNTs, the lesionectomy alone failed to control seizures. These results could be explained by the wider epileptogenic zone. The only significant predictor for favorable seizure outcome was an absence of preoperative generalized seizures.

Conclusions. In children with extratemporal DNTs the results suggest that complete lesionectomy alone without invasive presurgical investigations are effective for long-term seizure control. For children with temporal DNTs not invading the amygdalohippocampal complex, extensive presurgical evaluations seem indicated. The absence of preoperative generalized seizures was associated with a better seizure outcome. (DOI: 10.3171/PED/2008/1/3/206)

KEY WORDS • amygdalohippocampectomy • dysembryoplastic neuroepithelial tumor • epilepsy surgery • lesionectomy • long-term outcome

DYSEMBRYOPLASTIC neuroepithelial tumors are a relatively recent and distinct entity first described by Daumas-Duport et al.6 in 1988. These tumors are commonly associated with epilepsy and constitute a heterogeneous group. Adjacent cortical dysplasia is found in most cases.6,26 Some authors have suggested that DNTs are frequently associated with a wider area of epileptogenic activity related to the presence of malformations in cortical development around the tumor. Invasive preoperative investigations are recommended for accurate localization of the epileptogenic zone.23,26

The surgical strategies for treating DNTs remain controversial. Some authors have reported good long-term seizure control after lesionectomy.12,23 In contrast, Aronica and colleagues1 found significantly lower levels of seizure control after lesionectomy compared with results after lesionectomy and amygdalohippocampectomy.

In the present study, we investigate the long-term seizure outcome after noninvasive presurgical investigations and the use of different surgical strategies in children with DNT-related epilepsy.

Clinical Materials and Methods

Patient Selection

Between May 1986 and May 2006, 27 children with DNTs underwent operations at the Department of Pediatric Neurosurgery, University Hospital La Timone, Marseille. Patients included all children with a histopathological diagnosis of DNT who had undergone both pre- and postoperative imaging studies, and for whom postsurgical follow-up longer than 1 year was available. Presurgical investigations included MR imaging in all children, scalp EEG in 21 patients, video-EEG recordings in 6, stereo-EEG in 1, and neuropsychological testing in 6 children. We excluded patients who had previously undergone operations at other institutions (2 patients) or who had undergone biopsy sampling alone (1 patient). Under these criteria, 24 patients were eligible for this retrospective study.

Abbreviations used in this paper: DNT = dysembryoplastic neuroepithelial tumor; EEG = electroencephalography; MR = magnetic resonance.
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Study Parameters

We reviewed medical records for data including sex, age at seizure onset, age at surgery, seizure type and pharmacoresistance, lesion location, extent of resection, histopathological findings, seizure and antiepileptic drug usage, outcome, and tumor recurrence.

The lesion location was assessed in all cases on preoperative MR imaging. We classified temporal location as medial temporal (temporal tumors involving at least 1 of the following mesial structures: uncus, parahippocampal gyrus, amygdala, or hippocampus) and lateral temporal (without involvement of mesial structures). Regarding the involvement of the central region, the suprasylvian tumors were defined as frontal, frontocentral, parietocentral, and parietal.

The child’s preoperative epilepsy status was defined as medically resistant if seizures remained disabling despite application of at least 2 antiepileptic drugs for a period longer than 1 year. The resections were classified as complete lesionectomy, partial lesionectomy, and lesionectomy with amygdalohippocampectomy. Extent of resection was assessed in all cases with postoperative imaging—computed tomography and/or MR imaging.

The DNTs were diagnosed and classified according to the definitions of Daumas-Duport et al. The simple form of DNT lacks a specific glioneuronal element; the complex form is composed of the specific glioneuronal element with multiple glial nodules; and the nonspecific form of DNT lacks a specific glioneuronal element and is characterized by partial seizures with an onset before 20 years of age, no neurological deficits or stable congenital deficits, cortical topography, no mass effect, and no edema on neuroimaging.

The seizure outcome was assessed at 1 year, 2 years, and at the last follow-up examination using the Engel classification system.9

Statistical Analysis

We analyzed continuous variables with t-tests and categorical variables with the chi-square test and Fisher exact test. Probability values < 0.05 were considered significant.

Results

General Characteristics

The patients included 18 boys and 6 girls. The age at surgery in these patients was 1–15 years (mean 8.9 years), and the age at seizure onset ranged from the neonatal period to 13 years (mean 6.3 years). The mean duration of epilepsy was 3.4 years (0.25–14 years). The follow-up period was 1–16 years (mean 6.7 years). The other general characteristics of our patients are presented in Table 1.

Seizure Outcome and Follow-Up

In our patients, surgical treatment resulted in Engel Class I seizure control in 20 (83.3%) of 24 children at 1 year postoperatively and in 20 (90.9%) of 22 patients at 2 years. Two children had only 1 year of follow-up. There were 20 patients (83.3%) with Class I seizure control at the last follow-up examination. Seizure outcomes are summarized in Table 2.

Table 1: General characteristics of lesions and epilepsy in 24 children with DNTs

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>pharmacoresistant epilepsy</td>
<td>12</td>
</tr>
<tr>
<td>presence of generalized seizures</td>
<td>9</td>
</tr>
<tr>
<td>tumor location</td>
<td></td>
</tr>
<tr>
<td>medial temporal</td>
<td>10</td>
</tr>
<tr>
<td>lateral temporal</td>
<td>5</td>
</tr>
<tr>
<td>frontofrontal</td>
<td>2</td>
</tr>
<tr>
<td>frontal</td>
<td>2</td>
</tr>
<tr>
<td>parietales</td>
<td>1</td>
</tr>
<tr>
<td>temporoparietal</td>
<td>2</td>
</tr>
<tr>
<td>parietal</td>
<td>1</td>
</tr>
<tr>
<td>occipital</td>
<td>1</td>
</tr>
<tr>
<td>interictal EEG findings*</td>
<td></td>
</tr>
<tr>
<td>concordant w/ lesion</td>
<td>19</td>
</tr>
<tr>
<td>distant to lesion</td>
<td>2</td>
</tr>
<tr>
<td>histopathological findings</td>
<td></td>
</tr>
<tr>
<td>simple form</td>
<td>17</td>
</tr>
<tr>
<td>complex form</td>
<td>4</td>
</tr>
<tr>
<td>nonspecific form</td>
<td>3</td>
</tr>
<tr>
<td>associated malformation of cortical development</td>
<td>4</td>
</tr>
<tr>
<td>residual tumor after op</td>
<td>1</td>
</tr>
</tbody>
</table>

| * Data available in 21 cases. |

Table 2: Engel Class seizure outcomes at 1 year, 2 years, and at the last follow-up

<table>
<thead>
<tr>
<th>FU (no. of children)</th>
<th>Class I</th>
<th>Class II</th>
<th>Class III</th>
<th>Class IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 yr (24)</td>
<td>20</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2 yrs (22)</td>
<td>20</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>last (24)*</td>
<td>20</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

* The mean duration of follow-up was 6.7 years (range 1–16 years). The 2 children with only 1 year of follow-up are included in this category. Abbreviation: FU = follow-up.
because of tumor involvement of amygdala and hippocampal head. In another child the hippocampus was included in the epileptogenic zone and resected after stereo-EEG recordings. Two of the 6 children who did not undergo amyg
dalohippocampectomy had Engel Class III seizure control.

Prognostic Factors

The comparison between children with favorable outcomes (Engel Class I) and children with incomplete seizure control (Classes II and III) regarding other prognostic factors is presented in Table 3. The only significant predictor of a favorable seizure outcome was the absence of preoper
ergative generalized seizures.

Antiepileptic Drugs Outcome

Complete antiepileptic drug withdrawal was achieved in 12 children (50%). Medical treatment remained unchanged in 7 patients, and the doses were decreased in 2 patients, and increased in 1 patient. The medical treatment was changed postoperatively in 2 children because of persistent seizures.

Cognitive Outcome

This study is retrospective, and therefore neuropsychological evaluations were not systematically performed in the first patients included in this series. Neuropsychological evaluation was performed in 4 children with medial temporal DNTs, 1 child with a lateral temporal DNT, and in 1 child with an extratemporal lesion. All 5 children with temporal tumors remained seizure free after surgery. Two young children (a 2-year-old and a 3-year-old) who were severely developmentally retarded preoperatively continued to have moderate cognitive deficits 3 and 4 years after surgery. In the other 3 children, the preoperative cognitive level was normal and was not altered by surgery. Surgical strategies in the 5 children with available neuropsychological assessment consisted of lesionectomy with left amygdalohippoc
campectomy in 3 cases (in 2 children with medial temporal DNTs involving the hippocampus and 1 child with amygdalohippocampectomy after stereo-EEG) and lesionectomy alone in 2 children. One child with an extratemporal DNT had a normal pre- and postoperative cognitive level.

Tumor Control

One child had 2 recurrences after complete resection, as documented on postoperative MR imaging. Another child had residual tumor that remained stable 4 years after surgery as shown on surveillance MR imaging.

Postoperative Complications

There were transient complications in 5 children (20.8%): 1 child had a motor deficit, 1 child had mild apha
sia, 2 children had third cranial nerve palsies, and in 1 child a bone flap infection developed which requiring flap re
moval and cranioplasty. Major complications occurred in 4 children (16.7%): 2 had persistent mild motor deficits, and 2 children had hemianopsia.

Discussion

Seizure Outcome

In our series, 83.3% of children had Engel Class I seizure control 1 year after resection, 90.9% at 2 years, and 83.3% at the last follow-up (mean follow-up 6.7 years). In our review of the literature (Table 4) we found an incidence of Engel Class I seizure outcome after resection ranging from 52.4 to 100%.

Our data are consistent with the conclusion of other authors who argued that the run-down phenomenon after resection of DNTs was not significant.14 Luyken et al.10 reported a very stable percentage of seizure-free patients in a large series of long-term epilepsy-associated tumors. In contrast, Nolan and associates10 reported a high rate of seizures recurrence after surgery for epilepsy-associated DNTs. However, this rundown phenomenon was significantly as
associated with incomplete lesion resection2 and differs from the typical late recurrence described in the long-term follow-up of patients after resection for hippocampal sclerosis.19 Thus, if complete resection of DNTs was performed, the seizure-free outcome without the rundown phenomenon seems possible.

Preoperative Evaluation

Preoperative evaluations included obtaining a thorough seizure history and MR imaging studies in all patients and interictal scalp EEGs in all but 3 children. Ictal video-EEGs were performed in 6 children. Stereo-EEG was used in only 1 patient. This child had a medial temporal DNT and con
 tinued to have seizures despite complete lesionectomy. On stereo-EEG a residual epileptogenic zone located in the ad
jacent hippocampus was found. The patient underwent ad
ditional amygdalohippocampectomy and became seizure free.

Positron emission tomography, single photon-emission computed tomography, magnetencephalography, and inva-
Surgical strategy for pediatric DNTs

TABLE 4

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Patients</th>
<th>Tumor Localization</th>
<th>Intracranial EEG</th>
<th>Type of Op</th>
<th>Mean FU in Yrs (Range)</th>
<th>% w/ Engel Class I</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daumas-Duport et al., 1988</td>
<td>39</td>
<td>T, F, O, P</td>
<td>iEEG</td>
<td>LE, LE &amp; AHE</td>
<td>9.0 (1–18)</td>
<td>76.9</td>
</tr>
<tr>
<td>Kirkpatrick et al., 1993</td>
<td>27</td>
<td>T</td>
<td>ECoG</td>
<td>LE &amp; AHE</td>
<td>5.8 (1–14)</td>
<td>81</td>
</tr>
<tr>
<td>Raymond et al., 1995</td>
<td>21</td>
<td>T, O, F, P</td>
<td>—</td>
<td>LE, LE &amp; AHE</td>
<td>1.8 (0.2–14)</td>
<td>52.4</td>
</tr>
<tr>
<td>Davis et al., 1997</td>
<td>18</td>
<td>T, F, P</td>
<td>—</td>
<td>LE, LE &amp; AHE</td>
<td>2.7 (0.5–7)</td>
<td>77.8</td>
</tr>
<tr>
<td>Fomekong et al., 1999</td>
<td>16</td>
<td>T, F, P</td>
<td>—</td>
<td>NA</td>
<td>3.3 (1–3.3)</td>
<td>53.3</td>
</tr>
<tr>
<td>Lee et al., 2000</td>
<td>20</td>
<td>T, O, F, P</td>
<td>ECoG</td>
<td>LE, LE &amp; AHE</td>
<td>3.2 (1.1–10)</td>
<td>90.0</td>
</tr>
<tr>
<td>Aronica et al., 2001</td>
<td>13</td>
<td>T, O, F, P</td>
<td>iEEG</td>
<td>LE, LE &amp; AHE</td>
<td>5.0 (2.1–3.9) (1 case)</td>
<td>85.7</td>
</tr>
<tr>
<td>Fernandez et al., 2003</td>
<td>14</td>
<td>T, O, F, P</td>
<td>iEEG(1 case)</td>
<td>LE, LE &amp; AHE</td>
<td>7.3 (2.1–3.9)</td>
<td>86.0</td>
</tr>
<tr>
<td>Luykxen et al., 2003</td>
<td>25</td>
<td>T, O, F, P</td>
<td>iEEG</td>
<td>LE, LE &amp; AHE</td>
<td>8.0 (2–14)</td>
<td>86.0</td>
</tr>
<tr>
<td>Nolan et al., 2004</td>
<td>26</td>
<td>T, O, F, P</td>
<td>ECoG</td>
<td>LE</td>
<td>4.3 (1–11)</td>
<td>62.0</td>
</tr>
<tr>
<td>Sandberg et al., 2005</td>
<td>18</td>
<td>T, F, P, insula</td>
<td>iEEG, ECoG</td>
<td>LE, LE &amp; AHE</td>
<td>1.6 (0.02–10.5)</td>
<td>100</td>
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<tr>
<td>Chan et al., 2006</td>
<td>18</td>
<td>T, F, P</td>
<td>—</td>
<td>LE, LE &amp; AHE</td>
<td>10.8 (7.8–14.8)</td>
<td>66.7</td>
</tr>
<tr>
<td>present study</td>
<td>24</td>
<td>T, F, O, P</td>
<td>SEEG (1 case)</td>
<td>LE, LE &amp; AHE</td>
<td>6.7 (1–16)</td>
<td>83.3</td>
</tr>
</tbody>
</table>

* AHE = amygdalohippocampectomy; ECoG = electrocorticography; F = frontal; iEEG = invasive EEG; LE = lesionectomy; NA = not available; O = occipital; P = parietal; SEEG = stereo-EEG; T = temporal; — = not specified.
† Reported included 27 DNTs, 3 gangliogliomas, and 1 hamartoma.

Surgical Strategies

Complete lesionectomy without intracranial EEG recordings in children with extratemporal DNTs was sufficient to achieve seizure control in all 9 children. Sandberg and colleagues and Aronica et al. reported similar results after lesionectomy of extratemporal DNTs but recommended invasive EEG and electrocorticography. Other authors concluded that a large proportion of children with extratemporal lesions continue to have seizures despite lesionectomy. Davis et al. proposed 2 possible explanations for this phenomenon: incomplete DNT resection or persistence of the surrounding epileptogenic dysplastic cortex. In the present study, we achieved 100% seizure control after extratemporal complete lesionectomy without invasive EEG recordings, suggesting that the total resection plays a major role in seizure outcome.

Extratemporal epilepsies usually have a lower rate of postoperative seizure control than temporal ones. Some authors confirmed these findings in patients with DNT-related epilepsy. Our results differ from these reports because all of our patients with incomplete seizure control had temporal lesions.

All 4 children with complete lesionectomy and amygdalohippocampectomy were seizure free at the last follow-up examination. Lesionectomy alone was performed in 11 children with temporal DNTs, and this was insufficient to achieve complete seizure control in 4 cases. Davis et al. reported 100% seizure control after anterior temporal lobectomies in 12 patients with anterior temporal DNTs. Aronica and associates observed better seizure control in patients harboring temporal DNTs who were treated with lesionectomy and amygdalohippocampectomy compared with patients who underwent lesionectomy alone.

These data stress the importance of the amygdalohippocampectomy in the treatment of some temporal DNTs. Our technique of amygdalohippocampectomy using piecemeal resection and ultrasonic aspiration did not permit hippocampal histological examination. Aronica et al., Kirkpatrick et al., and Davis and coworkers found mesial temporal sclerosis in 0, 19, and 27% of patients, respectively. In their studies, the association of DNT and hippocampal sclerosis did not achieve significant value as a predictor of seizure outcome. We suggest that minimal hippocampal abnormalities probably explain better results after lesionectomy associated with amygdalohippocampectomy in patients with temporal DNTs.

Amygdalohippocampectomy is associated with risks of neuropsychological and vascular complications. Therefore, it seems that extensive presurgical evaluations should be performed before deciding on amygdalohippocampectomy in patients with temporal DNTs that do not involve the amygdala and/or hippocampus.

Prognostic Factors

In our patients, age at epilepsy onset, age at surgery, duration of epilepsy, preoperative EEG findings, histological forms of DNTs, and the presence of malformations of cortical development did not achieve significance as seizure predictors. We found a significantly better seizure outcome in children without preoperative generalized seizures. This is in agreement with other studies of seizure outcome after epilepsy surgery. Other factors predictive of a good outcome reported in the literature have included a young age at surgery, shorter seizure duration prior to surgery, and complete lesion resection. Our series and the other reported series have been relatively small; future studies with larger patient cohorts could help to better define the significant predictors for favorable seizure outcome.

Literature on Postoperative Antiepilepsy Drug Status

In the present study, antiepilepsy medication was stopped in 12 children (50%). Fomekong et al. reported successful drug discontinuation in 8 (53.3%) of 15 patients, Kirkpatrick et al. reported success in 13 (52.0%) of 25 patients, and Chan and colleagues reported successful discontinua-
tion in 10 (55.6%) of 18 patients. Authors of recent studies that included lesions of other histological diagnoses have reported 14–35% long-term drug withdrawal after surgery for epilepsy.15,27 These results suggest that surgery for DNT-related epilepsy is distinct and affords a higher rate of seizure control and antiepileptic drug discontinuation than surgery for other types of epilepsies.

Postoperative Complications

Complete resection of DNTs is considered to result in excellent seizure control, without mortality and with few complications.1,23 Very few complications have been described in the literature, and we found only 1 study that described surgical complications in detail. Kirkpatrick et al.16 reported a 39% rate of early transient postoperative complications and 13% permanent neurological deficit in their patients. We found transient postoperative complications in 20.8% of our patients and permanent deficits causing mild disabilities in 16.7%. These results reflect our surgical strategy, which aimed for complete lesion removal even in children with tumors involving the central region or visual pathways.

Conclusions

Our results suggest that complete lesionsectomy alone without invasive presurgical investigations is effective for long-term seizure control in children with extratemporal DNTs. For children with temporal DNTs that are not invading the amygdalohippocampal complex, extensive presurgical evaluations seem indicated. We achieved better seizure outcome in children who did not have a history of preoperative generalized seizures.

References


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Address correspondence to: Gabriel Lena, M.D., Department of Pediatric Neurosurgery, University Hospital La Timone, 264 Rue Saint-Pierre, 13385 Marseille Cedex 05, France. email: gabriel.lena@ap-hm.fr.