Surgical Issues in Managing Tumor-Based Epilepsy: Extent of Resection Outcomes, and Timing

December 2, 2012

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Disclosure

none
Learning Objectives

• To understand the predictors of seizure-freedom in surgical patients with brain tumors
• To understand factors which affect quality-of-life and cognition in patients with tumor-related epilepsy
Original Paper

Prevalence and Prognostic Significance of Epilepsy in Patients with Gliomas

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Table 3. Prevalence of epilepsy in the main histological subgroups of 1028 intracranial gliomas treated between 1980 and 1995

<table>
<thead>
<tr>
<th>Histology</th>
<th>Epilepsy prevalence*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glioblastoma (n = 512)</td>
<td>252 (49%)</td>
</tr>
<tr>
<td>Anaplastic gliomas (n = 137)</td>
<td>95 (69%)</td>
</tr>
<tr>
<td>Low-grade gliomas (n = 379)</td>
<td>322 (85%)</td>
</tr>
</tbody>
</table>

*P < 0.001, chi-square.
Epilepsy in Low-Grade Gliomas: The Impact on Cognitive Function and Quality of Life

Martin Klein, PhD, Nadine H. J. Engelberts, PhD, Henk M. van der Ploeg, PhD,
Dorothee G. A. Kastelein-Nolst Trenité, MD, PhD, Neil K. Aaronson, PhD,
Martin J. B. Taphoorn, MD, PhD, Hans Baaijen, MD, W. Peter Vandertop, MD, PhD,
Martin Muller, MSc, Tjeerd J. Postma, MD, PhD, and Jan J. Heimans, MD, PhD

Low-grade gliomas frequently are associated with epilepsy. The purpose of this study is to determine the impact of epilepsy and antiepileptic drug (AED) treatment on cognitive functioning and health-related quality of life (HRQOL) in these patients. One hundred fifty-six patients without clinical or radiological signs of tumor recurrence for at least 1 year after histological diagnosis and with an epilepsy burden (based on seizure frequency and AED use) ranging from none to severe were compared with healthy controls. The association between epilepsy burden and cognition/HRQOL was also investigated. Eighty-six percent of the patients had epilepsy and 50% of those using AEDs actually were seizure-free. Compared with healthy controls, glioma patients had significant reductions in information processing speed, psychomotor function, attentional functioning, verbal and working memory, executive functioning, and HRQOL. The increase in epilepsy burden that was associated with significant reductions in all cognitive domains except for attentional and memory functioning could primarily be attributed to the use of AEDs, whereas the decline in HRQOL could be ascribed to the lack of complete seizure control. In conclusion, low-grade glioma patients suffer from a number of neuropsychological and psychological problems that are aggravated by the severity of epilepsy and by the intensity of the treatment.

Ann Neurol 2003;54:514–520

“The increase in epilepsy burden that was associated with significant reductions in all cognitive domains except for attentional and memory functioning could primarily be attributed to the use of AEDs, whereas the decline in HRQOL could be ascribed to the lack of complete seizure control.”
Seizure characteristics and control following resection in 332 patients with low-grade gliomas

EDWARD F. CHANG, M.D.,1 MATTHEW B. POTTS, M.D.,1 G. EVREN KELES, M.D.,1 KATHLEEN R. LAMBORN, PH.D.,1,2 SUSAN M. CHANG, M.D.,1,2 NICHOLAS M. BARBARO, M.D.,1 and MITCHEL S. BERGER, M.D.1,2

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All LGG patients (N=332)

No Pre-operative Seizures (N=63; 19%)

Pre-operative Seizures (N=269; 81%)

Surgery
cortical location oligodendroglioma oligoastrocytoma

AED
generalized

Controlled (N=137; 51%)

Uncontrolled (N=132; 49%)

Gross total resection

Seizure-free: Engel I (N=169; 67%)

Rare Seizures: Engel II (N=44; 17%)

Meaningful Improvement: Engel III (N=19; 7%)

No Improvement: Engel IV (N=21; 6%)

simple partial seizures seizure history > 1 year temporal lobe

J Neurosurg 2009
Seizure characteristics and control following resection in 332 patients with low-grade gliomas

Edward F. Chang, M.D., Matthew B. Potts, M.D., G. Evren Keles, M.D., Kathleen R. Lamborn, Ph.D., Susan M. Chang, M.D., Nicholas M. Barbaro, M.D., and Mitchell S. Berger, M.D.

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Predictors of Seizure Freedom (Engel Class 1)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross Total Resection</td>
<td>16</td>
<td>2.2-124</td>
</tr>
<tr>
<td>Simple partial seizures</td>
<td>0.36</td>
<td>0.18-0.72</td>
</tr>
<tr>
<td>Seizures &gt;1 year duration</td>
<td>0.28</td>
<td>0.1-0.56</td>
</tr>
</tbody>
</table>

***Seizure recurrence after initial postop seizure control predicts tumor progression (time dependent Cox proportional hazards model and Landmark method, p=0.003)
Predictors of seizure freedom after resection of supratentorial low-grade gliomas

A review

Dario J. Englot, M.D., Ph.D., Mitchel S. Berger, M.D., Nicholas M. Barbaro, M.D., and Edward F. Chang, M.D.

Department of Neurological Surgery, University of California, San Francisco, California

J Neurosurg 2011

N=773, 20 published studies

<table>
<thead>
<tr>
<th>TABLE 3: Predictors of seizure freedom after tumor resection*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Factor</strong></td>
</tr>
<tr>
<td>-----------------------------------</td>
</tr>
<tr>
<td>medically controlled seizures</td>
</tr>
<tr>
<td>simple partial seizures</td>
</tr>
<tr>
<td>seizures for ≤1 yr</td>
</tr>
<tr>
<td>gross-total resection</td>
</tr>
</tbody>
</table>
Role of Extent of Resection in the Long-Term Outcome of Low-Grade Hemispheric Gliomas

Justin S. Smith, Edward F. Chang, Kathleen R. Lamborn, Susan M. Chang, Michael D. Prados, Soomee Cha, Tarik Tihan, Scott VandenBerg, Michael W. McDermott, and Mitchel S. Berger

Extent of resection strongly correlates with Overall Survival
Comparison of a Strategy Favoring Early Surgical Resection vs a Strategy Favoring Watchful Waiting in Low-Grade Gliomas

Asgeir S. Jakola, MD
Kristin S. Myrmel, MD
Roar Kloster, MD
Sverre H. Torp, MD, PhD
Sigurd Lindal, MD, PhD
Geirmund Unsgård, MD, PhD
Ole Solheim, MD, PhD

JAMA 2012
Take-home for LGG-epilepsy

Tumor control:
• GTR $\rightarrow$ 10 year survival $= 97$-$100\%$
• STR $\rightarrow$ 10 year survival $< 50\%$

Seizure control:
• GTR $\rightarrow$ seizure freedom $= 85\%$
• STR $\rightarrow$ seizure freedom $< 35\%$
Seizure control outcomes after resection of dysembryoplastic neuroepithelial tumor in 50 patients

Clinical article

Edward F. Chang, M.D., 1 Catherine Christie, M.D., 1 Joseph E. Sullivan, M.D., 2 Paul A. Garcia, M.D., 3 Tarik Thran, M.D., 3 Nalin Gupta, M.D., Ph.D., 1 Mitchell S. Berger, M.D., 1 and Nicholas M. Barbaro, M.D. 1

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TABLE 4: Multivariate predictors of seizure control outcome at 12 months*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Temporal Lobe Location</th>
<th>GTR/Extended Lesionectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td>1.20</td>
<td>1.68</td>
</tr>
<tr>
<td>95% CI</td>
<td>1.02–1.42</td>
<td>1.39–2.03</td>
</tr>
<tr>
<td>p value</td>
<td>0.03</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Long-term seizure control outcomes after surgery for Gangliogliomas

Southwell D, ... Chang EF  *Neurosurgery* 2012
Intractable epilepsy in paralimbic Word Health Organization Grade II gliomas: should the hippocampus be resected when not invaded by the tumor?

Clinical article

FADI GHAREEB, M.D.,¹ AND HUGUES DUFFAU, M.D., PH.D.,²,³

J Neurosurg 2012

N=15
All patients seizure-free with additional hippocampal resection
Also, all returned to work
Conclusions:

Decision-making for tumor-related epilepsy is more straightforward than non-lesional epilepsy surgery

Subtotal vs Gross-total resection is critical for seizure-freedom and long-term survival

Epilepsy surgery approach is more appropriate than tumor approach
  - Familiarity with intraop electrocorticography
  - Familiarity with mesial temporal structures/anatomy
  - Anatomic approach is better
  - Consideration of risks: memory/eloquence

Does pathology matter? Not really.
  - Outcomes nearly same for LGG/DNET/GG
Controversies:

**Timing**

If suspicion of glioma, then operate. Do not wait.
- up to 50% of non-enhancing tumors are anaplastic astrocytomas (worse prognosis, require chemo/radiation)
  - GG and DNET can be difficult to distinguish from LGG/AA
Controversies:

**Resection- how much to take?**

Temporal lobe: lesionectomy vs lobectomy?

Lateral temporal or insular: resect or spare hippocampus?

Extratemporal: lesionectomy vs extended lesionectomy (with intraoperative electrocorticography)?

Is there a role for chronic intracranial monitoring?
Controversies:

Resection- how much to take?

Medial temporal lobe: lesionectomy vs lobectomy?
- If refractory epilepsy → lobectomy

Lateral temporal or insular: resect or spare hippocampus?
- If epilepsy → resect hippocampus, intraop ECoG

Extratemporal: lesionectomy vs extended lesionectomy (with intraoperative electrocorticography)?
- Extended lesionectomy

Is there a role for chronic intracranial monitoring?
- NO, seizure localization rarely difficult; outcomes are excellent without it