Influence of Head Trauma on Outcome Following Anterior Temporal Lobectomy

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Background: There is controversy in the literature regarding the importance of risk factors in developing epilepsy and seizure outcome following anterior temporal lobectomy. Some of the existing studies may be biased because of patient selection and limitations in determining predisposition.

Objective: To investigate the role of risk factors for epilepsy in determining outcome following anterior temporal lobectomy.

Patients and Methods: We identified 102 patients in a consecutive surgery series for epilepsy from a tertiary center with a minimum of 1-year postoperative follow-up. Risk factors for epilepsy were determined prospectively on at least 3 occasions before anterior temporal lobectomy. Risk factors investigated were a history of febrile convulsions, family history of epilepsy, significant head trauma, history of meningitis, history of encephalitis, or significant perinatal insult. Foreign tissue lesions on magnetic resonance imaging was also included if an anterior temporal lobectomy was performed for presumed dual pathologic findings (hippocampus and lesion). Outcome was determined using Engel’s classification. For statistical analysis we used successive logistic regression analysis, $\chi^2$ test, Fisher exact test, and t test.

Results: Of the 102 patients, 13 had no identified risk factor for epilepsy, 49 had 1 identified risk factor, and 40 had more than 1. Frequencies were 39 febrile convulsions (15 complex febrile convulsions), 29 head trauma, 22 with lesions seen on magnetic resonance imaging, 12 history of meningitis, 2 history of encephalitis, 19 family history of epilepsy, and 4 perinatal insult. Seventy-one (70%) were classified as Engel’s class I, with 56 patients continuously free of seizures at follow-up. Those without risk factor were as likely to be rendered free of seizures following anterior temporal lobectomy as those with a risk factor ($P = .27$). No risk factor alone or in combination was correlated with complete freedom from seizures following anterior temporal lobectomy, but the presence of head trauma, alone or in combination, was correlated with continued seizures following anterior temporal lobectomy ($P = .03$; odds ratio, 2.6). Better outcomes were not seen in those with head trauma before the age of 5 years ($P = .57$). These findings did not change if all those with lesions on magnetic resonance imaging were excluded in the analysis. Those with a history of head trauma were as likely to have pathologic evidence of mesial temporal sclerosis as others ($P = .82$).

Conclusions: Patients with a history of significant head trauma are less likely to become free of seizures following anterior temporal lobectomy. No other risk factor correlated with a statistically significant greater or lesser chance of freedom from seizures. This information may be used in preoperative counseling of patients.

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PATIENTS AND METHODS

One hundred two patients with medically intractable complex partial epilepsy from a continuous series underwent ATL at the University of Michigan Hospital in Ann Arbor between June 1990 and March 1996. Seizure outcome was determined as of March 1997, a minimum of 1 year after surgery, using Engel’s classification. The best outcome, termed class Ia, is defined as complete freedom from seizures following ATL excluding early postoperative seizures. Continued need for anticonvulsants is not included in this definition. Patients were chosen for ATL based on criteria published elsewhere. The presence of individual risk factors did not influence ATL candidate selection.

Risk factors for epilepsy were determined from at least 3 structured interviews with each patient, family members, and close friends before surgery. Medical records were used, when available, to confirm and supplement information provided. All credible risk factors were included in this analysis. These included FC, significant head trauma (HT), history of meningitis, history of encephalitis, family history of epilepsy, and significant perinatal insult resulting in cerebral palsy or neonatal convulsions. These were chosen based on the work of Rocca et al, which describes risk factors for complex partial seizures from a population-based case-control study, and from a recent study by Berkovic et al. Those with complex FC (FC lasting ≥30 minutes, or with postictal focal neurologic deficits) were identified and analyzed both separately and grouped with simple FC. Head trauma with any of the features described by Rocca et al were included in the analysis: loss of consciousness, posttraumatic amnesia, or evidence of skull fracture. In their study, HT was significant even when loss of consciousness was less than 30 minutes in duration. Those with a foreign tissue lesion seen on magnetic resonance imaging (MRI) were included so as not to exclude those with presumed dual pathologic features (pathologic features in the lesion and hippocampus), who presumably will have seizures of mesial temporal lobe onset. The analysis was repeated excluding those with lesions seen on MRI to ensure that the findings of this study were not biased. Surgical pathologic findings were reviewed by one of us (M.B.), an experienced neuropathologist who was blinded to patient risk factors and surgical outcome. Results were categorized for ease of analysis, as showing mesial temporal sclerosis (>50% neuron loss in CA1), a foreign tissue lesion, mesial temporal sclerosis, and a lesion, or no pathologic diagnosis. For statistical analysis we used the SAS statistical software and Statview (SAS Inc, Cary, NC) to perform successive logistic regression analysis, χ² test, Fisher exact test, and t test.

RESULTS

Thirteen of the 102 patients had no identified risk factor for epilepsy. Of 89 with recognized risk factors, 40 had more than 1 identified risk. The frequencies of individual risk factors and the most common combinations are presented in Table 1.

Outcomes were as follows: 56 patients with class Ia (55%), 15 class Ib, Ic, or Id (15%), 12 class II (12%), 8 class III (8%), 10 class IV (10%), and 1 unavailable for follow-up. The percentage of frequencies of class Ia outcomes for the most common risk factors are listed below.

Table 1. Incidence of Risk Factors for Epilepsy*

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>13</td>
</tr>
<tr>
<td>FCs</td>
<td>19</td>
</tr>
<tr>
<td>Head trauma</td>
<td>10</td>
</tr>
<tr>
<td>Lesion seen on MRI</td>
<td>10</td>
</tr>
<tr>
<td>History of meningitis</td>
<td>6</td>
</tr>
<tr>
<td>FCs and family history of epilepsy</td>
<td>6</td>
</tr>
<tr>
<td>Family history of epilepsy</td>
<td>3</td>
</tr>
<tr>
<td>FCs and head trauma</td>
<td>3</td>
</tr>
<tr>
<td>FCs and meningitis</td>
<td>2</td>
</tr>
<tr>
<td>FCs and perinatal insult</td>
<td>2</td>
</tr>
<tr>
<td>Head trauma and lesion seen on MRI</td>
<td>2</td>
</tr>
<tr>
<td>Head trauma and family history of epilepsy</td>
<td>2</td>
</tr>
<tr>
<td>Family history of epilepsy and meningitis</td>
<td>2</td>
</tr>
<tr>
<td>Head trauma, lesion seen on MRI, and family history of epilepsy</td>
<td>2</td>
</tr>
<tr>
<td>FCs, head trauma, and family history of epilepsy</td>
<td>2</td>
</tr>
<tr>
<td>Febrile convulsions, head trauma, and family history of epilepsy</td>
<td>2</td>
</tr>
<tr>
<td>Febrile convulsions, lesion seen on MRI, and family history of epilepsy</td>
<td>2</td>
</tr>
<tr>
<td>Head trauma, perinatal insult, and family history of epilepsy</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>14</td>
</tr>
</tbody>
</table>

* MRI indicates magnetic resonance imaging; other, combinations of risk factors other than those individually listed.

There was no difference in likelihood of class Ia outcomes between those with and those without an identified risk factor (P = .27). Using sequential logistic regression analysis, no single risk factor for epilepsy, combination, or absence of risk for epilepsy was more likely than others to be associated with class Ia outcomes. The only correlation with outcome was HT that was negatively correlated with class Ia outcomes in this series (P = .03; odds ratio, 2.6). Given these initial results we investigated HT further and found a positive correlation between HT and class III outcomes (P = .002).

Subset analysis of those with HT revealed no difference in outcome between those whose injury occurred before or after the age of 5 years (P = .57). Data on outcome by age at HT are presented in Table 2. Length of follow-up was not longer for those with HT (mean ± SD, 46.7 ± 3.3
months) compared with others (mean ± SD, 43.5 ± 2.2 months) in this series. As this was a consecutive series it included those with bilateral temporal lobe epilepsy if 80% or more of ictal onsets were recorded from the same side. Eleven of 102 patients had bilateral temporal lobe epilepsy, 2 with a history of HT. There was no increased incidence of HT in those with bilateral temporal lobe epilepsy (P = .72). Thirty-four patients required invasive monitoring with depth and/or subdural strip electrodes before ATL, 8 had a history of HT. Those with HT were not more likely to require invasive presurgical monitoring in this series (P = .44). Preoperative MRI was reviewed in those with HT and correlated with outcome. Five patients showed changes consistent with mesial temporal sclerosis, 14 were normal, 2 had foreign tissue lesions seen on MRI, 4 had nonspecific inflammatory or posttraumatic changes, 1 had focal atrophy, and 3 had hemosiderin deposition. Only the presence of hemosiderin correlated with outcome, with better seizure outcomes seen in this group (P = .04), but these data should be interpreted with caution because of the small sample size. Age at surgery did not differ between those with a history of HT (mean ± SD, 34.2 ± 6.3 years) and those without (mean ± SD, 31.9 ± 9.3 years) (P = .15, t test). Neither was there a difference between the 2 groups with respect to age at onset of epilepsy with a mean (± SD) of 14.9 ± 9.0 years for those with HT and a mean (± SD) of 12.1 ± 10.8 years for those without (P = .20, t test).

Eighty-nine of 102 pathologic specimens were available for review. Sixty-two showed mesial temporal sclerosis (alone), 10 dual pathologic features, 8 foreign tissue lesions without mesial temporal sclerosis, and 9 had no pathologic diagnosis. The only findings of significance were all those with a history of meningitis had mesial temporal sclerosis (P = .02) and, as expected, the presence of a lesion on MRI correlated with the presence of a lesion by pathologic review (P = .001). Twenty of 29 with HT had mesial temporal sclerosis by pathologic review, similar to all other risk groups with the exception of those with meningitis (P = .82).

Due to concerns about possible bias from inclusion of those with lesions seen on MRI, a repeated analysis was performed excluding these individuals. Head trauma remained the only significant risk factor with regard to outcome (P = .04).

In this study, which examined all accepted risk factors for epilepsy, whether present alone or in combination, and their relationship to outcome in a cohort of patients undergoing ATL for medically intractable complex partial epilepsy, we found no correlation between individual risk factors and complete freedom from seizures following ATL. Those without an identified risk factor for epilepsy were no less likely than any other group to be rendered free of seizures after surgery for epilepsy. Only a history of HT correlated with outcome. Those with HT, whether alone or in combination with other risk factors, were less likely to become free of seizures following ATL, and more likely than any other group to have class III outcomes (worthwhile improvement with more than “rare” seizures, which we operationally defined as up to 80% reduction of seizures and usually meant continued monthly seizures). These poorer outcomes cannot be explained by histopathologic absence of mesial temporal sclerosis. Those with a history of HT at a young age did not have better outcomes than those with later HT. Patients with HT were not more likely to have bilateral temporal epilepsy based on preoperative ictal recordings, require invasive ictal monitoring, or show differences from other risk groups in age at onset of epilepsy, age at surgery, or length of follow-up. Of those with HT, preoperative MRI findings consistent with hemosiderin deposition correlated with freedom from seizures following ATL.

These results are different from the findings of Abou-Khalil et al who found in a consecutive ATL series an association between prolonged FC and good outcome after surgery. This may be due to differences in the way risk factors for epilepsy were evaluated. In their study, patients were separated into those with and those without FC. Other risk factors were determined in each of these groups, and in their review 39% of the non-FC group had a history of HT, while only 10% of the FC group had a similar history. The authors noted that HT was statistically significant in predicting poor outcome following ATL (P = .03), however they concluded that this was less important than the presence of FC. This decision was made on the basis of absolute P values rather than a statistical analysis that compared both factors. Another difference between the 2 studies is the definition of good outcome that included all class I outcomes in their review. From a physician standpoint this is not unreasonable, but increasing data from quality-of-life measures and long-term employment status after surgery for epilepsy support a real separation between those completely free of seizures and even those with continued simple partial seizures after ATL.

Our finding that those without an identified risk factor for epilepsy did as well as those with a known risk is in agreement with that of early investigators, but contrasts with that of Mathern et al. There are differences in how outcome was defined between the 2 studies and when outcome was determined, but despite this, fewer than 25% of their study population without a risk factor for epilepsy were free of seizures in the last 12 months of follow-up. In our series nearly 70% of those without a risk for epilepsy were continuously free of seizures for the duration of follow-up, between 13 to 70 months. These differences may be due to different patient populations, or due to differences in preoperative patient selection as all our patients had the benefit of MRI and functional imaging with positron emission tomography before surgery, and the time frame of patient ac-

Table 2. Outcome by Age at Head Trauma

<table>
<thead>
<tr>
<th>Age at Head Trauma, y</th>
<th>Ia</th>
<th>Ib, Ic, Id</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>≥5</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>

* No difference in outcome was seen between those with head trauma before and after 5 years of age (P = .57).
†Engel’s classification.
quisition in the study by Mathern et al. precluded such an evaluation for all their patients.

The absence of a positive correlation between individual risk factors and good outcome following ATL is, we believe, due to the overall high success rate of ATL, especially in light of current surgical selection criteria that now include MRI and functional imaging. With a procedure for which the chances of long-term complete success are higher than 50%, it is likely that studies of large numbers of patients will be necessary to show any statistically significant difference between those patients who do well and those who are continuously free of seizures. Fifty-five percent in this series had class Ia outcomes. As we reported, continuous outcome since ATL, rather than outcome in the most recent 12 months of follow-up or at some specific point of time after surgery, our results do not differ significantly from long-term outcome reported by others. We note, however, that the sample size of some etiologic groups was small (ie, meningitis, encephalitis, or perinatal insult) and conclusions regarding outcome among these should be viewed with caution.

Animal models of HT using fluid percussion injury have shown that even mild unilateral HT results in bilateral (ipsilateral greater than contralateral) neuron loss in the hilus and CA3 region of hippocampus, and enhanced limbic epileptogenesis. It is possible that bilateral mesial temporal injury may account for the poorer outcomes seen in those with HT; however, this does not appear to be the case in this population based on preoperative assessment, and would not be unique to HT as most mesial temporal lobe epilepsy appears to be bilateral with asymmetric severity irrespective of the cause of epilepsy based on autopsy series. The nature of the injury in HT may result in 1 or more of the following: multiple ictal onset zones where only the most active zone was resected, activation of a previously latent ictal onset zone occurs postoperatively, the presence of neocortical temporal lobe epilepsy simulating mesial temporal lobe epilepsy, or that HT injures subcortical structures that do not in themselves act as ictal onset zones, but which modulate or regulate cortical epileptic excitability, such that new ictal onset zones develop after surgery for epilepsy because these subcortical structures remain. As shown in animal models, it may be differences in the histopathologic features of mesial temporal structures in those with HT, with maximal neuronal loss in CA3 and absence of mossy fiber sprouting, which account for the poorer outcomes seen in this etiologic group.

Marks et al. reported a series of patients with a history of HT and outcome following surgery for epilepsy, not limited to ATL, and reported good outcome only in those whose trauma occurred before 5 years of age. Their overall impression, however, was that those with HT who had epilepsy that was difficult to localize, and in general deterred surgical intervention in this group. We did not find any difference in outcome comparing groups with HT before and after the age of 5 years. Once again study design may account for some of these differences. The Yale series excluded patients with any other possible risk factor for epilepsy.

In summary, in a cohort undergoing ATL, we found no single risk factor for epilepsy, whether the sole risk or combined with other risk factors, was predictive of complete freedom from seizures following ATL. Those undergoing ATL without an identified risk factor for epilepsy are not less likely to be rendered free of seizures following surgery. Those with a history of HT, whether the sole risk factor for epilepsy or combined with other risk factors, are significantly less likely to be rendered free of seizures following ATL, regardless of the age of injury. This information may be used in preoperative counseling of patients.

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REFERENCES