Epilepsy & Behavior 69 (2017) 24–27

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Brief Communication

Surgical outcome in adolescents with mesial temporal sclerosis: Is it different?

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ARTICLE INFO

Article history:
Received 14 July 2016
Revised 12 October 2016
Accepted 12 October 2016
Available online 20 February 2017

Keywords:
Adolescents
Mesial temporal sclerosis
Epilepsy surgery
Outcome

ABSTRACT

There are extensive studies evaluating mesial temporal sclerosis (MTS) in adults and limited studies in children, with adolescents being included within both patient populations. Our aim was to evaluate predictors of surgical outcome solely in adolescent patients with MRI- and pathology -proven MTS.

The Yale Epilepsy Surgery Database was reviewed from 1987 to 2012 for adolescent patients with confirmed MTS on MRI and pathology who underwent temporal lobectomy and had greater than two-year postsurgical follow-up. Clinical and electrographic data were reviewed. Eighteen patients were identified.

Eleven patients (61%) were seizure-free. All seven patients (39%) who were not seizure-free free were found to have lateralized ictal onset within one hemisphere involving two or more lobes on scalp EEG ($p < 0.001$). Of the 7 patients who were not seizure-free, 4 had a history of status epilepticus (compared to 1/11 seizure-free patients; $p = 0.047$), and 4 had lateralized hypometabolism involving two or more lobes within a hemisphere seen on PET (compared to 0/8 seizure-free patients; $p = 0.002$).

A novel finding in our study was that lateralized (rather than localized) ictal onset on scalp EEG, lateralized hypometabolism on PET, and history of status epilepticus were risk factors for not attaining seizure freedom in adolescents with MTS who underwent temporal lobectomy.

1. Introduction

Temporal lobe epilepsy is the most common type of epilepsy, accounting for 60% of focal epilepsies with the majority of these patients having mesial temporal sclerosis (MTS) [1–2]. Patients with this type of epilepsy with continued seizures despite two adequate trials of antiepileptic drugs are defined as having medically refractory seizures and warrant surgical treatment [3]. Surgical outcome has been reported to be favorable, ranging from 60 to 100% seizure freedom after resection [4–10]. Previous reports evaluating predictors of surgical outcome in patients with MTS have shown that dual pathology, bilateral MTS, normal MRI, longer duration of epilepsy, bilateral temporal epileptiform discharges, and history of secondary generalized seizures are associated with a lower chance of seizure freedom [4–10]. There have been extensive studies evaluating patients with MTS in adults with limited studies in children. Adolescents have been included within both patient populations [4–6,9].

Children frequently will have associated dual pathology with MTS likely contributing to their earlier age of seizure onset as well as higher seizure frequency [1,5], whereas adolescents and adults have higher incidences of isolated MTS without dual pathology [1]. Given these differences we hypothesized that adolescents with MTS likely would have different surgical outcomes than adults or children given their shorter duration of epilepsy from adults and lack of dual pathology as seen in children. Predictors of surgical outcome may also change as seizures evolve with time, increasing in frequency, possibly leading to repeat activation of epileptic networks which may alter surgical success. Our aim was to evaluate predictors of surgical outcome solely in adolescent patients with proven MTS on both MRI and pathology. Evaluating changes within surgical outcome as well as predictors of surgical outcome through the years from childhood to adulthood was beyond the scope of this study.

2. Methods

The Yale Epilepsy Surgery Database was reviewed from 1987 to 2012 for adolescent patients (age 12–18 at time of surgery) with confirmed MTS on MRI and pathology who underwent a standard temporal lobectomy (TL) and had greater than two-year postoperative follow-up. MTS on pathology was defined as gliosis and neuronal loss within the hippocampus, and specifically CA1. Patients with dual pathology or lack of follow-up data were excluded from the study. Dual pathology was defined radiographically as the presence of any lesion in addition to MTS on MRI and

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http://dx.doi.org/10.1016/j.yebeh.2016.10.028
1525-5050/

pathologically as a histopathologic abnormality other than gliosis and neuronal loss seen within the hippocampus and lateral temporal neocortex. The maintenance of the database and the methods of this study were are approved by the Yale Human Research Protection Program. Once these patients were identified, their clinical, demographic, and electrophysiological data were collected. Clinical information regarding age of seizure onset, duration of epilepsy, seizure frequency, and type, length of post-surgical follow-up, current and history of antiepileptic drug (AED) use, history of status epilepticus (SE), along with epilepsy risk factors including febrile seizures (FS) with or without febrile status epilepticus (FSE), was gathered. Information regarding secondary generalized seizures (GTCs) that had occurred during their lifetime not in association with fever or solely on initial presentation, along with presence and type of aura, was also gathered. Auras were classified as sensory, psychic, autonomic or motor. SE was reported in the chart as defined by the clinician occurring at any time point during the patient's history of epilepsy. FS were defined as provoked seizures secondary to fever in a child older than 1 month but <6 years of age without history of afebrile seizures [11]. FSE was defined as a FS lasting >10 min [11]. Imaging studies with Positron Emission Tomography (PET) were reviewed when available and hypometabolism on PET was described as either localized if confined to one lobe, or lateralized if it involved two or more lobes within one hemisphere. Electrographic data evaluated were interictal and ictal findings on scalp EEG, as well as intracranial EEG if performed. The decision for performing an intracranial study was made by the clinician as a consensus at the weekly surgical conference after reviewing the patient's clinical history along with imaging, electrographic, and neuropsychological data. Interictal epileptiform discharges on scalp EEG were described by location within a specific lobe (temporal, frontal, parietal, occipital) as well as side (right or left). If the interictal discharges occurred only within one hemisphere of the brain then it was deemed unilateral, and if within both hemispheres, then bilateral. Scalp ictal onset was described as either localized if the initial ictal rhythms occurred within one lobe or lateralized if the ictal rhythms occurred as hemispheric onset involving two or more lobes. Intracranial EEG ictal onset was classified by the specific region within a lobe where ictal rhythms were first detected. Surgical outcome was based on the ILAE classification and categorized as seizure-free (ILAE Class I–II) and not seizure-free (ILAE III–VI). Statistical analysis was performed using the Fisher's exact and backward logistical regression.

3. Results

In our center's surgical population from 1987 to 2012, a total of 34 adolescent patients underwent a temporal lobectomy. Of those 34 patients, 22 patients had MTS, 9 patients had gliomas, 2 patients had dual pathology, and 1 patient had no lesion. In contrast to the 22 adolescent patients with MTS who underwent temporal lobectomy, a total of 259 adult patients with MTS underwent temporal lobectomy during the same time frame at our center. Median age for surgery at our center is 31 with a median duration of epilepsy being 25.05 years.

Eighteen adolescent patients had greater than two-year post surgical follow-up data available, with 11 being female and 7 being male. Four patients were lost to follow-up, not returning to clinic or responding to inquiries regarding surgical outcome post-operatively. Median age of seizure onset was 5 years with a range of 0.5–12 years. Median age at surgery was 16 years with post-surgical follow-up ranging from 2 to 18 years (median 7 years). Duration of epilepsy ranged from 2 to 17 years with a median of 10 years, with the majority of patients (15/18) having either daily or weekly seizures pre-surgery. Eleven patients had left MTS, six had right MTS, and one had bilateral MTS. The majority of patients (16/18) had an aura prior to their seizures with all being sensory auras, including 13/16 patients with epigastric sensations. Nine patients had secondarily generalized seizures occur during their lifetime not in association with fever or solely on initial presentation of seizures. Eleven patients (61%) were seizure-free, with 2 patients being off AEDs and the majority (63%) on one AED at last follow-up. Seven patients (39%) were not seizure-free, with a majority of them being on three AEDs at time of last follow-up. The median number of AEDs patients were taking prior to surgery was 5, with a range of 3–7 AEDs. Fourteen patients had interictal epileptiform discharges on EEG with 13/14 having unilateral temporal spike wave discharges. Table 1 contains the clinical and electrographic data for all patients.

There were no patients with non-lateralized seizure onset on scalp EEG and ictal onsets always occurred on the same side as the MTS. All 7 patients (39%) who were not seizure-free were found to have lateralized (rather than localized) ictal onset on scalp EEG, compared to 0/11 patients who were seizure-free ($p < 0.001$). Ictal onset pattern for 14/18 patients was rhythmic theta with 4/7 of the non-seizure-free group having this pattern at seizure onset (NS). Nine patients underwent intracranial EEG monitoring and all were found to have localized seizure onset within the medial temporal lobe, including 6 patients within the non-seizure-free group who had lateralized scalp EEG onset. Five patients had a history of SE with four occurring at time of seizure onset. Four patients with history of SE did not achieve seizure freedom, and this rate of SE (4/7) was significantly higher than that seen in seizure-free patients (1/11; $p = 0.047$). Three of these 4 patients had SE in the setting of a febrile illness with no known etiology, and one in the setting of receiving chemotherapy for systemic lymphoma. Half of these patients presented with focal motor SE at the time of seizure onset and all presented with SE above the age of 8.

Of the 18 patients, only one had a history of FSE and was seizure-free post-surgery. Twelve patients underwent PET imaging: 8 displayed localized temporal hypometabolism and 8/8 became seizure-free; 4 showed lateralized hypometabolism (more than one lobe) and 0/4 became seizure-free ($p = 0.002$). Electrographic pattern at seizure onset, presence of bilateral interictal epileptiform discharges, bilateral MTS, and history of FS, FSE or GTCs were not found to be statistically significant in predicting surgical outcome. In addition, we deployed a backward logistic regression model to determine the most significant variables affecting surgical outcome. It was found that lateralized onset on scalp EEG was the most significant factor associated with poor surgical outcome. Table 2 illustrates the statistically significant factors associated with surgical outcome.

4. Discussion

MTS is the most common lesion seen in the temporal lobe for both adolescents and adults with refractory partial-onset epilepsy and is the most common reason to undergo epilepsy surgery within both these age groups [2]. Previous studies on predictors of surgical outcome for patients undergoing TL for MTS have included adolescents within either the adult or pediatric cohort of patients. We specifically wanted to study predictors of surgical outcome on adolescents to evaluate if the predictors are similar or different than those seen in children or adults. Given that adolescents are a unique population with specific psychosocial demands, additional information regarding predictors of surgical outcome could potentially be beneficial in counseling these patients prior to surgery, specifically in regards to driving and employment. At our center, the number of adult patients undergoing TL for MTS was found to be ten times that of adolescents during the same time period, with a median age of 31 at time of surgery with median duration of epilepsy being 25 years. This discrepancy in numbers between the adult and adolescent patients undergoing surgery for MTS along with the duration of epilepsy being >20 years is potentially illustrative of the delay to surgical treatment and may explain the low sample size of our cohort of adolescent patients.

The majority (61%) of adolescent patients with MTS who underwent temporal lobectomy in our study were seizure-free, as seen previously in other studies [4–9]. However, our study did not find that epilepsy duration, bilateral MTS, bilateral epileptiform discharges, history of FS, FSE or GTCs had any influence on surgical