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Age at onset in patients with medically refractory temporal lobe epilepsy and mesial temporal sclerosis: Impact on clinical manifestations and postsurgical outcome

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ABSTRACT

Purpose: To evaluate the demographic and clinical manifestations and postsurgical outcome of childhood-onset mesial temporal sclerosis and temporal lobe epilepsy (MTS-TLE) and establishing the potential differences as compared to the patients with adult-onset MTS-TLE.
Method: In this retrospective study all patients with a clinical diagnosis of medically refractory TLE due to mesial temporal sclerosis, who underwent epilepsy surgery at Jefferson comprehensive epilepsy center, were recruited. Patients were prospectively registered in a database from 1986 through 2014. Postsurgical outcome was classified into two groups; seizure-free or relapsed. Clinical manifestations and outcome were compared between patients with childhood-onset MTS-TLE (i.e., age at onset of the first afebrile habitual seizure below 10 years) and those with adult-onset MTS-TLE (i.e., age at onset of the first afebrile habitual seizure 20 years or above).
Results: One hundred and twelve patients had childhood-onset MTS-TLE and 76 had adult-onset MTS-TLE. Demographic, clinical, EEG and MRI characteristics of these two groups were similar. Postoperative outcome was not statistically different between these two groups of patients ($P = 0.9$).
Conclusion: Temporal lobe epilepsy due to mesial temporal sclerosis is a common cause of epilepsy that can start from early childhood to late adulthood. The etiology of MTS-TLE may be different in various age groups, but it seems that when mesial temporal sclerosis is the pathological substrate of TLE, clinical manifestations and response to surgical treatment of patients are very similar in patients with childhood-onset MTS-TLE compared to those with adult-onset disease.

1. Introduction

Focal epilepsies account for about two-thirds of all adult epilepsy patients, and temporal lobe epilepsy (TLE) is the most common type of focal epilepsy [1,2]. Mesial temporal sclerosis (MTS) is the most common pathological substrate of TLE [3]. Temporal lobe epilepsy (TLE) with MTS is one of the most common types of medically refractory epilepsy referred for epilepsy surgery; it is often refractory to antiepileptic drugs (AEDs), but responds favorably to surgery [1,4].

In children, MTS is considered an infrequent etiology of epilepsy, but with the advances in diagnostic technologies, it has started to be diagnosed at an increasingly younger ages [5,6]. Besides, even in many adults with MTS-TLE a detailed clinical history will clarify that the age at onset of the habitual seizures was in childhood [7]. It has been previously reported that, older age at onset of epilepsy predicts better prognosis in patients with TLE [8].

The aim of this study was to evaluate the demographic and clinical manifestations of childhood-onset MTS-TLE and establishing the potential differences as compared to manifestations observed in adult-onset MTS-TLE. We also investigated the surgery outcome in childhood-onset MTS-TLE in comparison with that in adult-onset MTS-TLE.

2. Methods

In this retrospective study all patients with a clinical diagnosis of medically refractory TLE due to mesial temporal sclerosis, who underwent epilepsy surgery at Jefferson comprehensive epilepsy center, were recruited. Patients were prospectively registered in a database from 1986 through 2014. The diagnosis of MTS-TLE was made by the epileptologists working at this institution and based on clinical grounds (semiology), electroencephalographic (EEG)

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findings and imaging [magnetic resonance imaging (MRI)]. There was no age limit to enter the study. For all patients, a comprehensive presurgical evaluation including a 1.5 T brain MRI (epilepsy protocol) was performed. Magnetic resonance imaging studies were analyzed by neuroradiologists with expertise in epilepsy. Electroencephalographic (EEG) localization was considered unilateral if interictal and ictal EEG findings pointed to one side and considered as bilateral if either interictal or ictal EEG was bilateral or they were discordant. We classified patients as having childhood-onset MTS-TLE, if the age at onset of the first afebrile habitual seizure was below 10 years and adult-onset MTS-TLE, if the age at onset of the first afebrile habitual seizure was 20 years or above. We classified patients as having MTS if they had clear signs of mesial temporal atrophy and/or sclerosis in their MRI. Patients with normal MRI and those with dual pathology were excluded from this study.

All patients were submitted to surgical treatment (i.e., anterior temporal lobectomy). They all had to be under the care of an epileptologist at our institution for at least 1 year, postoperatively. They were followed for up to 5 years after their surgery. Postsurgical outcome was classified into two groups; seizure-free or relapsed. Aura was not considered as a relapse; only postoperative tonic–clonic seizures and complex partial seizures were considered as relapse.

Age, gender, race, epilepsy risk factors (e.g., febrile seizure, family history of epilepsy, etc.), age at seizure onset (i.e., the first afebrile habitual seizure), seizure type(s), EEG findings and MRI findings, date of surgery, date of the first relapse (if any) and date of the last contact with all patients were registered routinely.

Demographic variables and relevant clinical variables were summarized descriptively to characterize the study population. All variables were compared between patients with childhood-onset versus those with adult-onset MTS-TLE. Pearson Chi-square, Fisher's exact, Mantel–Cox and *t*-test were used for statistical analyses. Time to event analysis was used to produce a Kaplan–Meier estimate of seizure recurrence. Odds ratio and 95% confidence interval (CI) were calculated. *P* value less than 0.05 was considered as significant. This study was conducted with the approval by Thomas Jefferson University Review Board.

3. Results

Two-hundred eighty-one patients in our database had MTS-TLE with at least 1 year of postoperative follow-up. Age at onset of their habitual afebrile seizures is shown in Fig. 1. One hundred and eighty-eight patients were eligible for this study (89 males and 99 females). One hundred and twelve patients had childhood-onset MTS-TLE and 76 had adult-onset MTS-TLE. Demographic characteristics of these two groups are shown and compared in Table 1. Clinical characteristics of these two groups are shown and compared in Table 2. Odds ratio of having history febrile seizures in patients with childhood-onset MTS-TLE compared to those with adult onset disease was 3.1 (95% CI: 1.6–6). Electroencephalographic (EEG) characteristics of these two groups are shown and compared in Table 3. The EEG localization of the epileptogenic zone was not differently distributed in these two groups of patients ($P = 0.2$). Imaging (MRI) characteristics of these two groups are shown and compared in Table 4. The MRI localization of the epileptogenic zone was not differently distributed in these two groups of patients ($P = 0.07$). Finally, postoperative outcome was not statistically different between these two groups of patients ($P = 0.9$) (Fig. 2). The duration of postoperative follow-up was 4.2 ± 1.2 years in the first group and 4 ± 1.4 years in the second group; it was not statistically different between these two groups ($P = 0.2$). Epilepsy duration before surgery in patients with childhood-onset disease was 30 ± 12 years and in those with adult-onset epilepsy was 13 ± 9 years ($P = 0.0001$). However, this is a biased comparison as we had already dichotomized the patients based on their age at the disease onset.

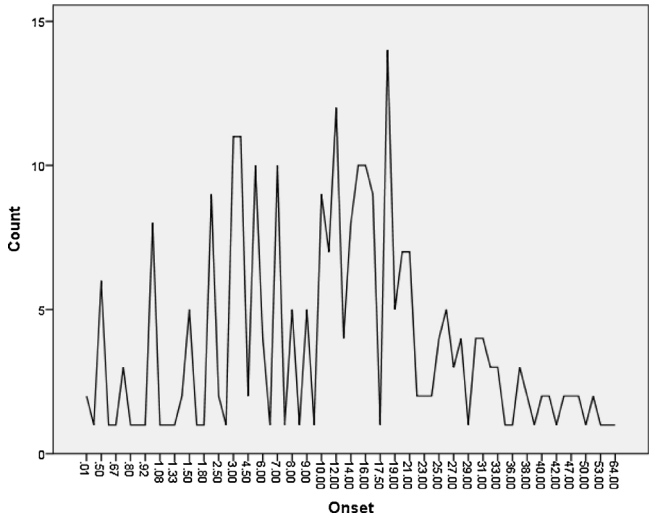

Fig. 1. Mean age at onset of all 281 patients was 15 ± 13 years. Minimum age at onset was the neonatal period and maximum age was 64 years.

Table 1
Demographic characteristics of patients with childhood-onset MTS-TLE compared to those with adult-onset MTS-TLE.

Demographic characteristic	Patients with childhood-onset MTS-TLE ($N = 112$)	Patients with adult-onset MTS-TLE ($N = 76$)	*P* value
Gender (male/female)	55/57	34/42	0.6
Race[a] (White/Hispanic/Black/Asian/Others)	94/3/10/1/2	62/1/9/2/0	0.5

TLE, temporal lobe epilepsy; MTS, mesial temporal sclerosis.
[a] Some data was missing.

Table 2
Clinical characteristics of patients with childhood-onset MTS-TLE compared to those with adult-onset MTS-TLE.[a]

Clinical characteristic	Patients with childhood-onset MTS-TLE ($N = 112$)	Patients with adult-onset MTS-TLE ($N = 76$)	*P* value
Seizure types[b] (CPS only/TCS only/CPS + TCS)	35/5/71	28/4/43	0.6
Aura[c] (none/epigastric/affective/mnemonic/others/multiple)	25/27/8/4/35/12	28/12/3/2/19/12	0.2
Remote history of tonic–clonic seizures (not within the past year)[d]	39 (34.8%)	26 (34.2%)	0.6
Recent history of tonic–clonic seizures (within the past year)[d]	37 (33%)	18 (23.7%)	0.2
History of status epilepticus	15 (13.4%)	7 (9.2%)	0.6
Family history of epilepsy	45 (40.1%)	22 (28.9%)	0.1
History of febrile convulsion	53 (47.3%)	17 (22.4%)	0.002

TLE, temporal lobe epilepsy; MTS, mesial temporal sclerosis; CPS, complex partial seizure; TCS, tonic–clonic seizure.
[a] Some data was missing.
[b] With or without auras.
[c] Not having aura was more common among patients with late-onset MTS ($P = 0.03$), but various types of auras were almost similarly reported by both groups (all *P* values >0.1).
[d] Compared with those who did not have history of tonic–clonic seizures.