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Comparison of temporal lobe epilepsy with hippocampal sclerosis and temporal lobe epilepsies due to other etiologies

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Abstract

Background: This study compares the clinical characteristics of patients with mesial temporal lobe epilepsy with hippocampal sclerosis (mTLE-HS) with those who have temporal lobe epilepsy (TLE) due to other etiologies.

Methods: In this retrospective study all patients with a clinical diagnosis of TLE were recruited in a referral outpatient epilepsy clinic at Shiraz University of Medical Sciences from September 2008 to May 2013. We classified the patients with TLE as having mesial temporal sclerosis if they had clear signs of mesial temporal sclerosis and/or atrophy in their MRI and others who had any other MRI abnormality.

Results: A total of 174 patients were studied (including 105 patients with mTLE-HS and 69 patients with TLE due to other etiologies). Frequency of seizure types was not significantly different between these two groups. Earlier age at epilepsy onset (p= 0.005), a past history of febrile seizures (p= 0.010) and presence of affective auras (p= 0.008) were commonly seen in patients with mTLE-HS, while auditory auras (p= 0.020) were more frequent in those with TLE due to other etiologies.

Conclusion: The mainstay for making a correct diagnosis, when evaluating a patient with seizure, is having a standardized approach, particularly with regard to taking a detailed clinical history. One may find important clues in the clinical history (e.g., age at disease onset, detailed seizure description and past history) to make a correct diagnosis.

Keywords: Age; Aura; Febrile seizure; Temporal lobe epilepsy; Hippocampal sclerosis.

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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). Temporal lobe epilepsy is subcategorized as mesial (i.e., amygdalohippocampal) and neocortical (i.e., lateral) temporal. Mesial temporal sclerosis is the most common pathological substrate of TLE (1,3). Mesial temporal lobe epilepsy (mTLE) with hippocampal sclerosis (HS) is one of the most common types of epilepsy referred for surgical treatment; it is often refractory to antiepileptic drugs (AEDs), but responds favorably to surgery (1,4). Patients with mTLE-HS and intractable seizures often experience progressive behavioral changes including increasing memory deficit with the passage of time. In addition, surgical outcome may be worse with longer duration of epilepsy or increasing age at surgery, which suggests that mTLE-HS is a progressive disorder (5). Therefore, early detection of this syndrome and its distinction from other TLE syndromes has im-

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portant practical implications with regard to planning an optimal treatment strategy for the affected patient.

In the current study, we tried to compare the clinical characteristics of patients with mTLE-HS with those who had TLE due to other etiologies in order to identify potentially differentiating clinical characteristics between these two groups of patients.

Methods

In this retrospective analytic study all patients with a clinical diagnosis of TLE were recruited in an outpatient epilepsy clinic at Shiraz University of Medical Sciences, which is the only referral epilepsy clinic in south Iran. This study was conducted from September 2008 to May 2013. The diagnosis of TLE was made exclusively by one epileptologist working at this institution (the first author) and based on clinical grounds (semiology), electroencephalographic (EEG) findings and imaging, such as magnetic resonance imaging (MRI). All patients were followed up by the epileptologist at our institution for at least one year (i.e., until May 2014). There was no age limit to enter the study. Routine EEG was requested for all patients at the time of referral. In difficult-to-diagnose or difficult-to- treat patients we often order video-EEG monitoring to ascertain the diagnosis and formulate an individualized treatment plan, accordingly. For all patients, a 1.5 Tesla brain MRI (epilepsy protocol) was performed.

Patients with normal MRI were excluded from this study. We classified patients as having MTS (if they had clear signs of mesial temporal sclerosis and/or atrophy in their MRI) and those who had any other MRI abnormality. Patients with dual pathology (i.e., mesial temporal sclerosis associated with other structural lesions) were excluded from the study.

Age, gender, age at seizure onset (i.e., the first afebrile seizure), seizure type(s), epilepsy risk factors (including pregnancy complications, history of febrile seizure, CNS infection, significant head trauma, positive family history of epilepsy), EEG findings (the most informative EEG), and MRI findings of all patients were registered routinely. Seizure types were categorized as generalized tonic clonic seizures (GTCS), complex partial seizures (CPS) and auras. Patients with concomitant psychogenic non-epileptic seizures (PNES) were excluded.

Demographic variables and relevant clinical variables were summarized descriptively to characterize the study population. Pearson Chi-Square, Fisher's Exact, and Mann-Whitney U tests were used for statistical analyses. P value less than 0.05 was considered as significant. This study was approved by Shiraz University of Medical Sciences Review Board.

Results

Until May 2014, 2890 patients with epilepsy were registered at our epilepsy clinic. Four hundred twenty-seven patients (14.7%) were diagnosed as having TLE. Of these, 174 patients were eligible to enter the study (105 patients with mTLE-HS and 69 patients with TLE due to other etiologies). Demographic and clinical characteristics of patients with mTLE-HS and those who had TLE due to other etiologies are shown and compared in table 1. Frequency of seizure types (i.e., GTCS vs. CPS vs. auras) was not significantly different between these two groups (Table 1). Specific types of auras were significantly different between these two groups (Table 1), however most auras were reported by both groups, similarly. Epilepsy risk factors were reported to be as follows (mTLE-HS vs. others): parental consanguinity in 41 / 30 (p= 0.6), family history of epilepsy in 18 / 10 (p= 0.6), significant head trauma in 15 / 7 (p= 0.4), CNS infection in 2 / 2 (p= 0.6) and pregnancy complications in 2 / 3 (p= 0.3).

Video-EEG monitoring was available in 155 patients; and 19 patients had a routine EEG only. We analyzed the most informative EEG. Eleven patients (10.4%) with mTLE-HS and four (5.8%) with other etiologies had normal EEG (p= 0.2). Right sided, left sided or bilateral focal epilepti-

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Table 1. Patients with mTLE-HS compared with those who had TLE due to other etiologies.

Characteristic	Patients with mTLE-HS	Other TLE patients	p
Gender (Male/Female)	49 / 56	36 / 33	0.4
Age at onset (years)	14.8 ± 9.5	19.9 ± 12.1	0.005
History of generalized tonic-clonic seizures	69 (65.7%)	51 (73.9%)	0.2
History of complex partial seizures	92 (86.3%)	55 (79.7%)	0.1
History of aura (single / multiple)	46 / 26	32 / 10	0.2
History of epigastric auras	28 (26.6%)	13 (18.8%)	0.2
History of mnemonic auras	20 (19%)	13 (18.8%)	0.9
History of affective auras	19 (18.1%)	3 (4.3%)	0.008
History of autonomic auras	12 (11.4%)	6 (8.6)	0.5
History of cephalic auras	3 (2.8%)	5 (7.2%)	0.2
History of visual auras	3 (2.8%)	2 (2.8%)	1
History of olfactory auras	3 (2.8%)	1 (1.4%)	1
History of gustatory auras	1 (0.9%)	3 (4.3%)	0.3
History of auditory auras	0	4 (5.8%)	0.02
History of febrile seizure	28 (26.6%)	8 (11.6%)	0.01
Focal interictal EEG abnormality	94 (89.5%)	65 (94.2%)	0.2
Uncontrolled seizures	64 (60.9%)	41 (59.4%)	0.8
Duration of follow-up (years)	2.7 ± 1.2	2.6 ± 1.1	0.3

mTLE-HS: Mesial temporal lobe epilepsy (mTLE) with hippocampal sclerosis (HS).

form discharges (i.e., temporal seizures, spikes or sharp waves) were observed in 36, 38, and 20 patients with mTLE-HS and 31, 21 and 13 patients with other etiologies, respectively (p= 0.4). Focal polymorphic delta activity or temporal intermittent rhythmic delta activity (TIRDA) was seen in 60 and 7 patients with mTLE-HS, respectively. These figures were 32 and 4 in patients with other etiologies (p= 0.3).

Magnetic resonance imaging (MRI) in patients with other etiologies (non- mTLE-HS group) showed temporal lobe tumors in 27 patients (39.1%), non-specific white matter MRI abnormalities in 11 (15.9%), cavernoma in seven (10.1%), sequels of head injury in six (8.7%), arachnoid cysts in five (7.2%) and other etiologies in 13 (18.8%) patients. Twelve patients had dual pathology (mesial temporal sclerosis in addition to another lesion). These were excluded from the study.

Discussion

Mesial temporal lobe epilepsy with hippocampal sclerosis is a common type of epilepsy referred for surgical treatment due to medical refractoriness. As a matter of fact, it responds very well to surgery (4). However, it has been suggested that early surgical intervention after seizure onset is an important precondition for achieving seizure-free status after surgery (6). Therefore, early detection of this syndrome has important practical implications with regard to planning an optimal treatment strategy for the affected patient, particularly those with medically-refractory seizures.

In the current study, we observed that earlier age at epilepsy onset (i.e., teenagers compared to young adulthood), a past history of febrile seizures and reporting affective auras (e.g., fear, anxiety, depression, joy, and anger) were commonly seen in patients with mTLE-HS, while auditory auras were more frequently reported by those with TLE due to other etiologies. Electroencephalography was not able to differentiate these syndromes of epilepsy from each another. In previous studies dominantly represented by patients with HS on MRI, it has been observed that age at onset is variable (7). The finding that age at onset is a potential clinical variable to distinguish mTLE-HS from TLE due to other etiologies should be further explored in future studies.

Several studies have shown a significant relationship between a history of febrile seizures in early childhood and mesial temporal sclerosis. In one study, it was observed that hippocampal T2 hyperintensity after febrile status epilepticus represents acute injury often evolving to a radiological appearance of HS after one year (8). Having a past history of febrile seizure is a use-

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ful historical clue in favor of mTLE-HS compared to TLE due to other etiologies.

As the first ictal symptoms, auras can provide important localizing and lateralizing information useful in determining the location of the epileptogenic zone (9). The observation that, affective auras (e.g., fear, anxiety, depression, joy, and anger) were commonly seen in patients with mTLE-HS, while auditory auras were more frequent among those with TLE due to other etiologies, has very important clinical implications. In one study, the authors examined the relationship between presence of different types of auras and post-surgical outcomes in 157 patients with medically intractable mesial temporal lobe epilepsy (mTLE) with unilateral hippocampal sclerosis (HS). The occurrence of multiple auras was not associated with post-surgical outcome ($p = 0.7$). But, the presence of extratemporal auras (e.g., somatosensory, visual and dysphasic auras) was significantly higher in patients with poor outcome (10). Designing future studies to investigate the relationship between presence of mesial temporal lobe auras (e.g., psychic symptoms, cognitive and affective auras, autonomic auras such as epigastric sensation, olfactory and gustatory auras) versus lateral temporal lobe auras (e.g., vertiginous and auditory auras) and surgery outcome in patients with mTLE-HS is necessary.

Conclusion

The mainstay for making a correct diagnosis, when evaluating a patient with seizure, is having a standardized approach, particularly with regard to taking a detailed clinical history. One may find important clues in the clinical history (e.g., age at onset, detailed seizure description and past history) to make a syndromic diagnosis. The syndromic diagnosis forms the basis for the treating physician to decide upon an appropriate management plan.

Limitations

This was a clinic-based series and may not represent the full spectrum of TLEs.

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Conflict of interest

Ali A. Asadi-Pooya has received honoraria from Cobel Daru. Others have no conflict of interest.

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