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## Benign mesial temporal lobe epilepsy: A clinical cohort and literature review

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#### ABSTRACT

Objective: We present a single-center retrospective study of benign mesial temporal lobe epilepsy (bMTLE) between 1995 and 2014.

Methods: Hospital records and clinic charts were reviewed. The clinical, Eelectroencephalographic (EEG), imaging features, and response to treatment with antiepileptic drugs (AEDs) were documented. Patients were included in this study if they were seizure-free for a minimum of 24 months with or without an AED.

Results: Twenty-seven patients were identified. There were 19 (70%) females, mean age at first seizure was 32.2 (range: 15-80 years). In all patients, seizures were mild, and seizure freedom was readily achieved with the initiation of AED therapy. Sixteen patients (59%) had mesial temporal sclerosis (MTS). In three patients, we attempted to discontinue AED therapy after a prolonged period of remission (5-8 years), but all had seizure recurrence within 2 to 4 weeks.

Significance: Not all temporal lobe epilepsy is refractory to medication, despite the presence of MTS. Until clinical trials indicate otherwise, surgery is not indicated but life-long medical treatment is advocated.

of MTS [2].

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#### 1. Introduction

Temporal lobe epilepsy (TLE) is the most common form of focal epilepsy in adulthood [1]. Among such patients, mesial temporal sclerosis (MTS, also called hippocampal sclerosis) is the most common underlying pathologic abnormality, as has been demonstrated in both autopsy and postresection studies [2].

Mesial TLE (MTLE) has long been considered an acquired, severe, drug-resistant form of epilepsy [3]. Recently, associations with both MTS and a history of prolonged febrile convulsions have been reported, both portending a worse prognosis [4,5]. As such, surgical resection of epileptic foci, is often considered. Reviewing the literature, however, it is clear that TLE is not a uniform disorder since, while many patients have a severe drug-resistant form, others have a much milder epileptic disorder and are able to achieve indefinite periods of remission either with or without antiepileptic drug (AED) therapy [6,7].

Relatively, little attention has been paid to these milder forms of TLE, including benign mesial temporal lobe epilepsy (bMTLE), despite the fact that this form of epilepsy was first documented almost a half century ago [8]. To qualify as bMTLE, a patient must have at least 24 months of seizure freedom, either with or without AED; moreover, seizure onset tends to

Corresponding author. E-mail address: dr\_alqasmi@yahoo.com (A. AlQassmi). explained away [10]. This paper describes the clinical, Eelectroencephalographic (EEG), and magnetic resonance imaging (MRI) findings in a cohort of patients with benign mesial TLE. Our goals were (1) to confirm the benign trajectory of this condition beyond the two-years of seizure freedom required for diagnosis and (2) to characterize this patient cohort with respect to its clinical, EEG, and imaging findings to confirm the relatively sparse published findings of others. We were especially interested in seeing whether our series would exhibit the same relatively high rate of MTS and low rates of other seizure risk factors reported elsewhere.

be later, usually well into adulthood [9,10]. Interestingly, however, roughly 40% of patients with long-standing bMTLE exhibit MRI evidence

Because a large percentage of studies on TLE have, to date, been

orchestrated by investigators with a special interest in its surgical

treatment, most currently-available information concerns patients

with refractory, nonlesional TLE. In some of these cases, risk factors for

epilepsy, like febrile convulsions and cerebral infections, can be identi-

fied, with MTS the most commonly recognized [11]. Conversely, milder

forms of TLE largely remain undefined entities from both an etiological

and electroclinical point of view. Some clinicians suggest that such

patients often remain undiagnosed, since many lack major seizures,

experiencing only transient focal seizures that are overlooked or









#### 2. Methods

A retrospective review was performed of all available clinical, EEG, and MRI data on patients meeting the criteria for bMTLE followed in the Outpatient Epilepsy Clinic at the London Health Sciences Centre in London, Ontario, Canada for a minimum of three years between the years 1995 and 2014. Our center is a tertiary care epilepsy center with 10 bed-monitoring units in London, Ontario, Canada. Therefore, the majority of our patients have drug-resistant epilepsy (DRE) who are referred to us for presurgical workup around (1059) cases of temporal lobe epilepsy whose been diagnosed in our hospital during that period. We aimed to compare this cohort to those with drug-resistant TLE population from our center for that period.

Potential cases were identified by reviewing clinic lists, with confirmation performed via a thorough review of hospital and clinic records.

To be eligible for the current analysis, all patients had to have been diagnosed with TLE in accordance with the classification criteria listed in the International Classification of Epileptic Syndromes [6–12], using seizure semiology to aid in the identification of a temporal lobe origin of seizures (e.g., dyscognitive seizures with autonomic and/or psychological symptoms or sensory phenomena, like olfactory or auditory hallucinations). To otherwise be eligible for inclusion in our analysis, patients also needed to meet the following criteria: (1) EEG evidence of interictal epileptic spikes and/or seizures originating from the anterior mesial temporal region(s) or evidence of MTS in MRI, (2) seizures well-controlled on AED over a minimum of two years, (3) no obvious indications for epilepsy surgery, like an epileptogenic tumor or potentiallyunstable or growing vascular anomaly, (4) no familial syndrome potentially associated with multiple epileptogenic lesions, like tuberous sclerosis or neurofibromatosis, and (5) the availability of all necessary baseline and follow-up clinical evaluation records, including initial and follow-up histories and physical examinations, and all EEGs and brain MRIs over the duration of observation. Once located, these records were reviewed thoroughly and systematically by the clinical research team to extract and record all data of interest.

The routine baseline evaluation of each patient followed in the Outpatient Epilepsy Clinic consists of a detailed medical and neurological history, including any history of recent or distant head trauma, recent febrile illnesses, prior cranial surgery, previously-identified intracranial tumors, current and past medications, and any family history of seizures, febrile seizures, or seizure-associated syndromes (e.g., neurofibromatosis). Patients also are always asked about the seizures they have had, including the patient's age at the time of their first seizure, the nature of that first seizure, including any precipitating event(s), the number of seizures they have had since then (roughly), the symptoms and frequency of their seizures, the presence/absence and nature of auras, whether generalization of focal seizures has ever occurred and how often, any AEDs administered, noting both their effectiveness and side effects, the response of the seizure to treatment.

In addition, patients have routine blood work to identify any additional risk factors for seizures, interictal Eelectroencephalogram (EEG), and magnetic resonance imaging (MRI) of the brain. Eelectroencephalograms (EEGs) are recorded using a 21-channel poly-graph, with electrodes positioned in compliance with the International 10–20 scalp electrode placement system for EEGs. Standard MRIs include T1- and T2-weighted, as well as FLAIR images in sagittal, coronal and axial planes, and are reviewed by an expert neuroradiologist.

Subsequent to the baseline evaluation and throughout the course of treatment, patients are followed regularly in clinic, including routine outpatient visits with an attending epileptologist, we see our patients every 3–6 months. At each assessment, a standardized evaluation is performed to collect data on the patient's seizures and medical and neurological status, followed by a targeted neurocognitive examination, and further investigations as indicated. In the current series, all patients had at least two routine outpatient EEGs at our institution.

Statistical analysis: As this is an observational study, descriptive analysis is included. Also, data are presented as group proportions or means with standard deviations, without further inferential analysis.

#### 3. Results

Over the duration of the observation window, a total of 27 patients were identified who satisfied inclusion criteria and were deemed eligible for further analysis. There were 19 females (70%), ranging in age of seizure onset from 15 to 80 years (mean =  $32.2 \pm 17.3$ ) (Table 1). Among these 27 patients, two experienced the onset of seizures prior to age 20 (15 and 19 years). Seizure onset in the remaining 25 was much later in life, ranging from 28 to 80 years of age. In our appraisal of the early records, we found that the diagnosis of TLE was always based upon the patient's clinical features, MRI and EEG, with the diagnostic criteria used similar to those described in the literature [10,13].

In 26 of the 27 patients, there was no known cause of seizures or precipitating clinical event. A single case was ascribed to possible viral encephalitis, but this diagnosis was based upon clinical history and the analysis of cerebrospinal fluid, with no virus ultimately detected. He was treated with acyclovir for >10 days, he was on phenobarbiton for 3 months and discontinued in that period because of the seizure that was reported. He was stable until he was presented with complex partial seizure at age of 15 years, seizure were controlled with carbamazepine, His EEG shows bilateral temporal slowing, his brain MRI was normal on two occasions, and as of his last outpatient visit, he was continuing to take a low dose of his medication out of concern that if seizure recurred he would lose his driver's license.

Two patients had experienced a febrile seizure at some time prior to the onset of their current seizures (partial seizure), and three patients reported a family history of febrile seizures. There also were three patients with a family history of seizures, including two families with additional cases of presumed benign TLE, albeit not currently being treated.

Seizures were clinically mild in all 27 patients at presentation, being either viscerosensory or associated with experiential auras in 22 patients (Table 1). Subsequently, but prior to initiating treatment, just over half (15 of 27, 55%) progressed to dyscognitive seizures associated

#### Table 1

Baseline demographic & clinical characteristic of 27 patients with benign temporal epilepsy.

Baseline demographic & clinical characteristics	N (%)	Characteristic of seizure	N (%)
N = 27		Symptoms	
Males	8 (29.6)	Viscerosensory or experiential auras	22 (81.5)
Females	19 (70.4)	Dyscognitive seizures Secondary generalization	15 (55.6) 5 (18.5)
Mean age	32.2 ± 17.3	Examination	- ()
Minimum age	15	Normal neurological examination	27 (100)
Maximum age	80	Normal cognitive examination	27 (100)
Early onset (<20 years)	2 (7.4)	History	0 (0.0)
Later onset (≥28 years)	25 (92.6)		
		Response to therapy	
An etiology of seizures		Controlled with medication	27 (100)
Viral encephalitis	1	Single drug therapy	23 (85.2)
Unknown	26	Multiple drug therapy	4 (14.8)
Risk factors for seizure			
Febrile seizures	2		
Family history	3		
Interictal EEG			
Normal	6 (22.2)	-	-
Unilateral abnormality	17 (63.0)		
Bilateral abnormality MRI	4 (14.8)		
Normal	11 (40.7)	-	-
Mesial temporal sclerosis	16 (59.3)		

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