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Misdiagnosis in JME: Still a problem after 17 years?

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ABSTRACT

Purpose: Juvenile myoclonic epilepsy (JME) is one of the most common and recognizable idiopathic generalized epilepsy with its characteristic clinical and EEG features. We think despite the well defined diagnostic criteria, and increasing awareness, misdiagnosis in JME may still be a problem. The present study aims to determine misdiagnosis in JME and to compare the results with our previous study reported in 1998.

Methods: Two hundred JME patients examined at epilepsy outpatient clinics of Bakirkoy Prof. Dr. Mazhar Osman Training and Research Hospital for Psychiatric, Neurologic and Neurosurgical Diseases between the years 2014–2015 were enrolled. Medical records of all patients were evaluated retrospectively; demographical, clinical and electrophysiological data and causes of misdiagnosis were collected from chart reviews.

Results: Of 200 JME patients, 49 were misdiagnosed at first medical evaluation. The most common presenting seizure types were generalized tonic clonic seizure and myoclonia in misdiagnosed patients and correctly diagnosed patients, respectively. EEG revealed generalized spike wave and polyspike-wave discharges in 52% of the misdiagnosed patients. Unfortunately the physician was a neurologist in 87.8% of cases with misdiagnoses. Nearly half of 49 misdiagnosed patients were prescribed an inappropriate antiepileptic drug, and the other half were prescribed none.

Conclusions: Comparing our new results with the ones in 1998, misdiagnosis rate was less and time to put a correct diagnosis was shorter. However, proper diagnosis at first sight is still a problem among neurologists even the typical EEG changes are present.

1. Introduction

Juvenile myoclonic epilepsy (JME) is one of the most common idiopathic generalized epilepsies of adolescence and early adulthood, characterized by myoclonic jerks, generalized tonic-clonic seizures (GTCS), and absence seizures [1,2]. The syndrome was first described by Janz in 1985 [3]. An international workshop on JME proposed two new sets of criteria in 2011 which will be helpful for both clinic and scientific purposes: "Class I criteria encompass myoclonic jerks without loss of consciousness exclusively occurring on or after awakening and associated with typical generalized epileptiform EEG abnormalities, with an age of onset between 10 and 25 years. Class II criteria allow the inclusion of myoclonic jerks predominantly occurring after awakening, generalized epileptiform EEG abnormalities with or without concomitant myoclonic jerks, and a greater time window for age at onset (6–25 years)" [4]. Despite the well defined diagnostic criteria, and increasing awareness of the disease, misdiagnosis in JME is still a problem. Unilateral myoclonic jerks and focal EEG discharges may lead to misdiagnosis of JME [5].

Juvenile myoclonic epilepsy responds dramatically well to treatment. However relapse rate is high after cessation of antiepileptic drugs (AED) (91%) [6–9].

The aim of our study is to determine difficulties in JME diagnosis and to compare the results with our related study reported 17 years ago.

2. Methods

Two hundred patients between 12 and 55 years of age and under the medical follow-up of epilepsy outpatient clinics in

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Bakirkoy Prof. Dr. Mazhar Osman Training and Research Hospital for Psychiatric, Neurologic and Neurosurgical Diseases in Istanbul, Turkey in 2014–2015 with a diagnosis of JME due to ILAE 2010 criteria were enrolled in this study [10]. Medical records of all patients were evaluated retrospectively and data were collected from chart reviews. Age, gender, family history of epilepsy, parental consanguinity, febrile convulsion history, age of seizure onset, seizure types, first seizure type, precipitating factors, delay time passed until the definite diagnosis, causes of delay, specialization of the physician who made the first visit, the first prescribed antiepileptic drugs, neurological examination findings, cranial magnetic resonance imaging (MRI), first EEG features (normal, generalized SW and PSW or/and focal abnormalities) and recent antiepileptic drug choices were noted. Participants were divided into two groups and compared as: the ones with a correct first diagnosis and the ones with a misdiagnosis at first.

The study was approved by Local Ethics Committee of Bakirkoy Prof. Dr. Mazhar Osman Training and Research Hospital for Psychiatric, Neurologic and Neurosurgical Diseases.

Continuous variables are expressed as the mean ± SD; categorical variables are presented as frequencies and percentages. The chi-square test was used to compare the differences in categorical variables between the groups. SPSS 17.0 statistical software was used for statistical analysis. A value of $p < 0.05$ was considered statistically significant.

3. Results

Of the 200 participants 57.5% ($n = 115$) were female. The mean age was 26.74 ± 8.46 (12–55 years). The mean age of seizure onset was 15.26 ± 4.1 (9–35 years).

First seizure types of patients were as follows: myoclonia in 54% ($n = 108$), GTCS in 42.5% ($n = 85$) and absence in 3.5% ($n = 7$). Seizure types recorded in follow up were solely myoclonia in 24.5% ($n = 49$), myoclonia and GTCS in 58.5% ($n = 117$), myoclonia and absence in 5% ($n = 10$), and myoclonia–absence–GTCS in 12% ($n = 24$) of all participants.

The most common factors of seizure precipitation were sleep deprivation in 36.5% ($n = 73$), stress in 34.5% ($n = 69$), fatigue in 28% ($n = 56$), emotional upset in 19.5% ($n = 39$), fasting in 13.5% ($n = 27$), photic stimulation in 13% ($n = 26$), excitement in 12.5% ($n = 25$), mental concentration in 11.5% ($n = 23$) and menstruation in 9.5% ($n = 19$) of patients.

Febrile convulsion was present in medical history of 11.5% ($n = 23$) of cases. In the family of 28% ($n = 56$) of the participants, there was at least one another patient with epilepsy. Neurological examination was found normal in all patients. The cranial MRI revealed cranio-vertebral junction abnormality (Chiari Type 1) in one patient. There was another patient with a focal demyelination. Apart from these, all of the MRI scans were normal in 198 patients.

First EEG revealed normal activity in 40.5% of patients ($n = 81$), generalized SW and PSW discharges in 34% of patients ($n = 68$), focal discharges in 18% of patients ($n = 36$) and both focal discharges and generalized SW and PSW discharges in 7.5% of patients ($n = 15$). Of all the focal discharges seen on EEGs, 70.5% ($n = 36$) were spikes from frontal areas and 29.5% ($n = 15$) were spikes from temporal areas (Table 1).

Hundred and fifty-one patients were diagnosed correctly at their first medical intervention. However, 49 patients were misdiagnosed. In 45 of 151 correctly diagnosed patients, the diagnoses were delayed due to late application to hospital and unawareness of first presenting seizure, when it was myoclonia. Of the 49 (24.5%) misdiagnosed patients the mean delay time until the correct diagnosis was 3.1 ± 4.1 (1–28) years.

Table 1
Clinical and demographical properties of JME patients.

	N:200	%
Gender (male/female)	85/115	42.5/57.5
Age (year)	26.74 ± 8.46 (12–55)	
Age of seizure onset (year)	15.26 ± 4.1 (9–35)	
First seizure type		
• Myoclonia	108	54
• GTCS	85	42.5
• Absence	7	3.5
Seizure type		
• GTCS and Myoclonia	117	58.5
• Myoclonia	49	24.5
• GTCS–Myoclonia–Absence	24	12
• Myoclonia and Absence	10	5
Febrile convulsion history		
• Yes	23	11.5
• No	177	88.5
Family history of epilepsy		
• Yes	56	28
• No	144	72
Parental consanguinity		
• Yes	39	19.5
• No	161	80.5
First EEG		
• Normal	81	40.5
• Generalize SW/PSW discharges	68	34
• Focal discharges	36	18
• Focal discharges and generalized SW/PSW discharges	15	7.5
MRI		
• Normal	198	99
• Chiari Type 1	1	0.5
• Demyelinating lesion	1	0.5
Recent AED treatments		
• Monotherapy	176	88
○ VPA	144	72.0
○ LEV	8	4.0
○ LTG	23	11.5
○ TPM	1	0.5
• Polytherapy	24	12

VPA: valproic acid, LEV: levetirasetam, LTG: lamotrigine, TPM: topiramate, GTCS: generalized tonic-clonic seizures, SW: slow wave, PSW: polyspike wave, AED: antiepileptic drugs.

Age of disease onset, parental consanguinity, presence of another epileptic family member, and febrile convulsion history were not significantly different in correctly diagnosed and misdiagnosed patient groups ($p > 0.05$). In the misdiagnosed group the first seizure that made the patients search for a medical care was a GTCS. However in the correctly diagnosed group most patients were applied to the hospital with myoclonia. This difference was significant ($p < 0.01$). Of the misdiagnosed patients, 28.6% ($n = 14$) had normal EEG, 10.2% ($n = 5$) had focal discharges, 53.1% ($n = 26$) had generalized SW and PSW discharges, 8.2% ($n = 4$) had both focal discharges and generalized SW and PSW discharges. The focal discharges seen on EEGs of misdiagnosed JME patients were spikes from frontal areas in 66.7% ($n = 6$) of cases and spikes from temporal areas in 33.3% ($n = 3$) of cases. Interestingly, generalized SW and PSW discharges were significantly more in patients misdiagnosed at their first medical contact and focal EEG discharges were significantly more in patients correctly diagnosed at their first medical contact ($p = 0.01$) (Table 2).

The physician who put the wrong diagnosis to 49 misdiagnosed patients in their first intervention, was a neurologist in 87.8% ($n = 43$), a general practitioner in 8.2% ($n = 4$), an internal medicine specialist in 2% and a psychiatrist in 2% of the cases. Of the 49 misdiagnosed patients, 22 had been prescribed AED, whereas 27 had been taken into follow up without any medication. The first seizure type and EEG results were not significantly different in between the patients that were prescribed with an AED and the ones that were not ($p > 0.05$).