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Clinical Presentations and Factors Responsible for Delays in Diagnosis of Juvenile Myoclonic Epilepsy among Sudanese Patients

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Abstract

Introduction: Juvenile Myoclonic Epilepsy (JME) is common idiopathic epilepsy manifested by myoclonic jerks that commonly noticed in early childhood without consciousness disturbance, then the generalised tonic – clonic overwhelms the scene, absence attacks are not uncommon. The prominent and cardinal EEG features of JME syndrome that supports the diagnosis is the generalized 3.5-6 Hz single, bifid and polyspikes slow-wave's complexes on normal brain background activity.

Aim: Aims were to evaluate the demographic features and to detect the most common clinical presentations among Sudanese patients with JME and explain the possible causes of diagnosis delaying.

Methods and patients: The study included all patients attended to National Ribat University – Faculty of Medicine and El-Magzoub Neurosciences centres whom their EEGs showed the characteristics features of JME (retrospectively). All the patients had been recruited (prospectively) and their EEGs have been repeated and clinical history and examination through pre-formed interview forms had bee done. The obtained data have been analysed using the SPSS and results were illustrated in by tables.

Results and discussion: The mean age of JME patients at diagnosis was 19.55 ± 8.98 years. Myoclonic jerks were confirmed in about 91% of the patients. Sleep deprivation was the triggering factor for MJs in 61.4% of the patients. Absence attacks were confirmed in 77.27% of JME patients, and generalised tonic-clonic seizures in 84.1% of patients with a mean age of onset 13.92 ± 5.65 years. The elapsed time between jerks and GTC was 4.35 ± 3.61 years.

Conclusion: MJs is common among Sudanese patients with JME and the sleep deprivation is the most frequent aggravating factors with the early awakening. Generalised tonic-clonic is common among JME patients and this great event may obscure MJs and confused the doctors to ask about them.

Keywords: Clinical presentations; Delayed diagnosis; Juvenile myoclonic epilepsy

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Introduction

The first official definition of JME is included in the ILAE classification of epilepsies and epilepsy syndromes [1]. This syndrome appears around puberty and is characterised by seizures with bilateral, single or repetitive, arrhythmic, irregular myoclonic jerks, predominantly in the arms. Some patients may suddenly fall from a jerk. No disturbance of consciousness is noticeable. Often, there are generalised tonic-clonic seizures (GTCS) and, less often, infrequent absences. The seizures usually occur shortly after awakening, and are often precipitated by sleep deprivation [2]. Interictal and ictal EEG have rapid, generalised, often irregular spike-waves and polyspikes-waves; there is no close phase correlation between EEG spikes and jerks. Frequently, the patients are photosensitive. Response to appropriate drugs is good [3]. Accordingly, JME includes three seizure types:

myoclonic jerks, GTCS and absences. In most patients, epilepsy begins around puberty with myoclonic jerks preceding the first GTCS for a mean period of 1.3 to 3.3 years [4]. In approximately 25% GTCS are observed before the myoclonic jerks, and in around one-third of the cases the major and minor seizures have simultaneous onset [4,5]. Myoclonic jerks in full consciousness, which are essential for the diagnosis, predominate in the upper limbs. They are spontaneous, brief, sudden, isolated or occur in brief arrhythmic clusters with characteristic Chrono dependence [6]. Generalised tonic-clonic seizures GTCS are present in 80% to 95% of JME patients and may follow a prolonged cluster of myoclonic jerks, with increasing amplitude and frequency, in a sequence that culminates in the tonic phase of an intense and particularly long GTCS [7]. Absences have been described in 31.9% of JME patients. In general, they are less frequent and short, and may be ignored by the patients due to incomplete, if any, impairment of consciousness [8]. Rarely, between 4.6% and 15% of cases, childhood absence epilepsy evolves into JME [6,9]. A good therapeutic response is part of the definition but could not always be confirmed [10]. On the other hand, there is a common belief that JME requires lifelong treatment because of an extremely high rate of relapse at attempts to terminate medication [7].

In this study we aimed to evaluate the clinical presentation for Sudanese patients with JME who have been diagnosed based on their EEGs findings and explain the possible causes of the delayed diagnosis.

Diagnostic Criteria of JME

Two diagnostic groups could have been established, one narrower and one wider. Class I criteria encompasses (i) myoclonic jerks without loss of consciousness exclusively occurring on or up to two hours after awakening; (ii) EEG with normal background and typical ictal generalized high amplitude polyspikes and slow waves accompanying myoclonic jerks; (iii) normal intelligence; and (iv) age of onset between 10 and 25 years [11]. The Class II set of criteria included (i) myoclonic jerks predominantly occurring after awakening; (ii) myoclonic jerks facilitated by sleep deprivation and stress and provoked by visual stimuli or praxis or GTCSs preceded by myoclonic jerks; (iii) normal background on EEG and at least one occurrence of interictal generalized spike or polyspikes and waves, with some asymmetry allowed, with or without recording of myoclonic jerks; (iv) no mental retardation or deterioration; and (v) age at onset of 6-25 years [11]. Our aims were to identify the clinical features of JME among Sudanese patients presented to National Ribat University and M S Elmagzoub neurophysiology and neurological centres and to explain different factors that may affect its diagnosis.

Patients and Methods

The study was conducted at the National Ribat University, Faculty of Medicine, and Department of Physiology, the EEG unit and M.S Elmagzoub Neurosciences Center, Khartoum State. The study includes all patients (3523 Sudanese patients) referred to the two centres during a period extended from March 2003 to May 2012. We included all patients that their EEG showed the characteristic findings of JME (generalized 3.5-6 Hz single, bifid and polyspikes slow - waves complexes on normal brain background activity [12]. We exclude from patients who had abnormal brain images, and or history of severe head trauma or obvious neurological deficit. Then patients had been recruited and an informed written signed consent had been obtained. A new EEG was done and detailed history and clinical examination had been done and 5 millimetres of venous blood withdrawn for a genetic study. Data have been analysed and demonstrated in form of tables **(Tables 1 - 6)** using the SPSS in the 21st edition.

Results

Out of 3523 patients attended to our clinics there were

Table 1 The classic EEGs findings of JME among patients with abnormal EEGs.

Patients Number (2063)	EEG findings
44	Generalised 3.5-6 Hz single , bifid and poly-spikes slow - waves complexes
44	Normal Cortical background activities

Table 2 Age at diagnosis of JME.

Age in years	Number of Patients	Percentage
<10	5	11.4
10 - <20	22	50.0
20 - <30	11	25.0
≥ 30	6	13.6
Min. – Max.	5.0 – 55.0	
Mean ± SD.	19.55 ± 8.98	
Median	18.0	

Table 3 Presence of myoclonic jerks, age of onset and time of occurrence among Sudanese JME patients.

Variables	No.	Percentage
Presence of Myoclonic Jerks	40	90.9
Age of Onset		
Mean ± SD	10.48 ± 4.81	
Time of Occurrence		
Early Morning	26	59.1
Day Time	22	50.0

Table 4 Jerks pattern, sites and associations among Sudanese JME patients.

Jerks Description	%
Cluster Jerks	80.0
Sporadic Jerks	20.0
Unilateral Jerks	34.1
Bilateral Jerks	36.4
Symmetrical Jerks	13.6
Affecting Shoulders	9.1
Upper Extremities	54.5
Lower Extremities	4.5
Entire Body	27.3
Associated with Falls	6.8
Loss of Consciousness	4.5

Table 5 The common triggering factors of myoclonic jerks among Sudanese JME patients.

Triggering Factor	%
Early Awaking	36.4
Sleep Deprivation	61.4
Emotional Stress	52.3
Alcoholic Drinking	0.0
Missed Dose	9.1
After a Nap	2.3
Phobic stimulation (TV)	13.6

Table 6 Generalized and absence seizures in Sudanese JME patients.

Seizure	No.	Percentage
Absence	34	77.27
GTC	37	84.1
Tonic	4	9.1
Clonic	6	13.6
Tonic-clonic	34	77.3
Age of Onset of GTC (Years) (n=37)		
Min. – Max.	2.0 – 29.0	
Mean ± SD.	13.92 ± 5.65	
Median	14.0	

2063 patients had abnormal EEGs (58.6%). Then and based on characteristic EEGs findings of JME; generalised 3.5-6 Hz single, bifid and polyspikes slow - waves complexes on normal brain background activity, the prevalence of JME was found to be 2.13% with moderate females' predominance (56.81%), compared to males (43.2%). The mean age of JME patients at diagnosis was 19.55 ± 8.98 years; the majority of patients (75%) were between 10 and 30 years. Myoclonic jerks were confirmed in about 91% of the patients with a mean age of onset 10.48 ± 4.81 years. As far as time is concerned; jerks occurred during early morning (59.1%) and in the day time (50%). Eighty percent of jerks occur in the form of clusters, while 20% were of the sporadic pattern. The upper extremities were affected in 54.5%, and the involvement of the entire body was observed in 27.3% of patient. Bilateral jerks were noticed in 36.4% of the patients and unilateral in 34.1%, some of the patients had more than one patterns. Sleep deprivation was the triggering factor for MJs in 61.4% of the patients , other frequent factors were emotional stress (50%) and early morning awakening (36.4%). Absence attacks were confirmed in 77.27% of JME patients, and generalised tonic-clonic seizures in 84.1% of patients with a mean age of onset 13.92 ± 5.65 years. Among patients with JME, the aura symptoms were negative in 91.9%, postictal sleepiness confirmed in 75.7%, but all patients lost their consciousness. The elapsed time between jerks and GTC was 4.35 ± 3.61 years. Five physicians (11.4%) referred their patients with JME as a possible diagnosis. Regarding the natal history of our patients, thirty-eight patients (86.4%) were delivered normally and 6 patients (13.6%) by caesarian sections and 27.3% of all patients experienced at least one febrile convulsions attack. Sleep disturbance was found in 40.9 %. About 79.5% of patients noticed deterioration in their memory capacities and 86.4% suffering of low school or work performance.

Positive family history of epilepsy was confirmed in 75% of the patients , 66.3% of them were first degree; while 33.7% were second-degree relatives.

Discussion

In the current study, 77.3% of Sudanese patients with JME had the JME triad symptoms at the time of the diagnosis, inconsistent with the result obtained by Murthy et al. [3] who found it only in 17.5% of patients with JME. Ninety present of Sudanese JME had myoclonic jerks in less than Ali et al. [13], those four patients in our study who denied the occurrence of myoclonic jerks were on AEDS that may obscure their jerks, as Panyiotobolous (8) stated. Myoclonic jerks in Sudanese patients triggered by sleep deprivation in 61.4% and emotional stress in 52.3%, partially accorded with Da Silva et al. results; 77% for sleep deprivation and 83% for stress. Photic stimulation and television watching were known stimulators of MJs in 13.5% of Sudanese patients. The present result is consistent with the observation of Da Saliva et al. [14]. All Sudanese JME patients denied alcohol consumption, although is a major trigger of MJs among JME patients (6, 14). Electroencephalography asymmetries have detected in 45.5% of patients in present study, higher than Montaleni (38.1%) [15] and lower than Letourneau (53.8%) [16] observations. The EEG records of 18.8% of Sudanese JME patients showed focal discharges accorded with Murthy et al. [3] observation. These EEG asymmetries, particularly the focal discharges are not uncommon in JME patients and many investigators accused them as the main cause of missed and delayed diagnosis. Only five physicians (11.4%) referred their patients to our centres labelling their request forms with JME. The mean delay of diagnosis of our patients was found to be 4.35 years; this result was in partial accordance with Vijai et al. [17] and Genton et al. [18]. It is apparent that the poor awareness about JME syndrome among Sudanese physicians has an immense role in JME missed a diagnosis, reflected in the form of the low prevalence and long mean delay time. This premise is confirmed by the success of increasing Spanish doctors awareness in decreasing the mean delay of JME diagnosis from 10.6 years in 1994 [19] to 2.4 years in 2001 [20]. The females represent 56.8% of Sudanese JME patients, against the declaration of ILAE [1] that states equal male to female ratio, but this female predominance accorded with most recent observations by Camfield [20] and Ali et al. [13]. An 88.6% Sudanese of patients with JME were diagnosed in their second decade of life, compatibles with the conclusion reached by Ali et al. [13] and the classic characterization of Janz [4]. The patients in the current study have wide age range (5 - 55 years), it is in line with Panyiotobolous results (2 - 40 years) [8], but the minimum and maximum ages are higher in Sudanese patients, embodies the great delay of diagnosis in Sudanese patients. In our patients the myoclonic jerks occur in clusters and mainly affecting the upper extremities (63.6%), their consciousness was preserved. These observations get along with Asconape and Penry [21] and Ali et al. [13] results. Two-thirds of Sudanese patients have absence seizures higher than a finding of Wirrell et al. [9]. The generalised tonic-clonic seizure is the cardinal complaint in 84.1% of Sudanese patients less than Ali

et al. observation (94.1%) [13]. In all Sudanese JME patients the GTCS followed the MJs by mean of 4.4 years compared to 3.3 years indicated by Asconape and Penry [21]. Ninety-two percent of Sudanese JME patients their GTCS seizures are not associated with aura symptoms. This finding may be explained by what Manganotti et al. [22] concluded, that the JME seizures are due to motor cortex hyperexcitability. Memory impairment has been mentioned by 79.5% of Sudanese patients with JME, elucidates the high percentage (86.4%) of patients who complain of work or school performance deterioration inconsistent with the determinations obtained by Vollmer et al. [23], Thomas et al. [24] and Lin et al. [25]. Among Sudanese JME patients 86.4% were delivered normally, and the rest of caesarian sections, but with unremarkable postnatal complications. This normal neonatal history ascertains the most important criterion of idiopathic epilepsy diagnosis proposed by Taylor et al. [26] and Engel [27]. Two-thirds of present patients have a family history of epilepsy; this finding supports the genetic assumption, documented by many investigators including Zifkin et al. [28] and Peljto et al. [29].

Conclusion

In spite of the fact that JME among Sudanese patients is a well recognised epileptic syndrome, both clinically by MJs and electronically still a lot of patients appear to be lost as missed diagnosis or at best it is diagnosis delayed for years. MJs is the cardinal presenting symptoms and usually aggravated by sleep deprivation and in almost all of the patients had GTCS at the time of EEGs investigation something reflecting the immense delay in diagnosis.

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