

CLINICAL EVALUATION OF 32 PATIENTS WITH JUVENILE MYOCLONIC EPILEPSY IN SOUTHERN KHORASAN

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ABSTRACT

Introduction: Juvenile Myoclonic Epilepsy (JME) is a frequent type of generalized seizure often associated with generalized tonic-clonic seizure (GTCS) and absence attacks. **Methods:** Consecutive patients with probable diagnosis of seizure referred to Valie-Asr and Emam Reza hospitals in southern Khorasan during March 2005-May 2007 were evaluated. Diagnosis of epilepsy and JME was made by neurologists based on clinical manifestations, history and EEG findings. Patients with structural brain lesions were excluded. **Results:** Of a total 396 epileptic patients, 32 JME cases (8.1%; 18 males, 14 females) were investigated. Mean age of JME onset and age at diagnosis were 12.4 years and 14.2 years, respectively; 27 patients with JME had GTCS and 7 patients had absence-type epilepsy. The triad of myoclonus, GTCS and absence spells was seen in only 4 cases while 2 cases had pure myoclonus. Myoclonic jerks were predominantly unilateral (or at least unilateral at onset) in 8 patients (25%). In 28 cases (87.5%), attacks predominantly occurred on awakening. Sleep deprivation was the most important precipitating factor, found in 26 cases (81.3%). Characteristic epileptic pattern of JME was found in 71.9% in the first EEG, which increased to 94% with repeat EEG. Positive family history for epilepsy was seen in 25%. **Conclusion:** JME is a frequent subtype of generalized epilepsy often associated with GTCS and absence. JME patients usually have a characteristic epileptic pattern on EEG.

Janz described Juvenile Myoclonic Epilepsy (JME) for the first time in 1957.¹ JME is frequently diagnosed in pediatric epilepsy clinics but is frequently not recognized by referring clinicians.² Myoclonic jerks often occur upon awakening in the morning or during early morning hours, which is characteristic for JME. Seizure types can vary within individuals and families with JME and other idiopathic generalized epilepsies.^{3,4,5} Typically, the patient is an otherwise healthy young teenager.⁶ JME is one of the most common types of generalized epilepsy and can be recognized by its characteristic clinical features. The electroencephalogram (EEG) reveals a 4 to 6 Hertz polyspike and wave discharge, which in a child with absence seizures may be indistinguishable from that of typical absence epilepsy.⁶ In 10 to 15 percent of JME patients, the initial EEG is normal.⁶ Repeat EEG should be

done in the morning after all-night sleep deprivation if the diagnosis of JME is in doubt. Although JME is classified as a generalized epileptic syndrome, focal epileptiform abnormalities on the EEG (up to 37 percent of cases in one series) are not uncommon, and some patients may have focal ictal symptomatology.^{7,8}

Approximately 20 to 30 percent of individuals with JME are photic sensitive on EEG (epileptiform activity and occasionally clinical myoclonus precipitated by repetitively flashing light), and some patients experience myoclonic jerks with video games. This report presents clinical, EEG and familial characteristics of JME in 32 cases seen in the two teaching hospitals of Birjand University of Medical Sciences.

MATERIALS AND METHODS

Consecutive patients with convulsive seizures were prospectively evaluated in Valie-Asr and Emam Reza hospitals, Birjand (Iran) during March 2005 - May 2007. These are the only centers in the southern Khorasan province with neurology services.

Clinical assessment, including history and neurological examination, of all patients was performed by a neurologist. Diagnosis of epilepsy was made based on the International League Against Epilepsy (ILAE) classification. Cases were only accepted as JME if they were independently confirmed by two neurologists based on the ILAE definition. These criteria include (a) unequivocal clinical evidence of generalized seizures with myoclonic jerks, mainly on awakening; (b) presence of absence seizure; (c) positive family history for JME; (d) normal neurologic examination; (e) characteristic EEG showing generalized spikes or multiple spike-and-slow-waves. Patients with organic brain insults or with history of myoclonus following head injury were excluded. Clinical data points included age, age at JME onset, gender, family history of JME, and lateralization (unilateral or generalized onset) of symptoms. Presence of other seizures (including GTCS and absence), use of anti-epileptic medication, seizure frequency, and seizure recurrence after termination of therapy, were also recorded. Additional factors considered include precipitating factors, circadian distribution, and family history of seizures. All patients underwent conventional inter-ictal EEG and brain imaging.

RESULTS

A total of 546 patients presenting with the complaint of seizures were investigated. Diagnosis of epilepsy was made in 396, of which 32 (18 males, 14 females; 8/1%) had JME. GTCS were found in 27 patients with JME (15 males and 12 females). Absence seizures were present in 7 cases with JME (4 males and 3 females). Mean age at diagnosis and at symptom onset was 14.2 years and 12.4 years respectively.

Myoclonus has not been as an isolated sign and other types of seizure activities - convulsive or nonconvulsive - have been seen with myoclonus in 93.7% of cases of JME. GTCS were seen in 27 (84.4%) of our JME cases. Seven cases (21.9%) with JME had absence seizures followed by myoclonic movements. Two of this latter group had some pure absence attacks but more often they experienced absence attacks followed by myoclonic jerks. Four (12.5%) of our studied cases had the triad of GTCS,

myoclonic jerks and absence. Two cases (6.25%) had pure myoclonus. In all studied cases we could find at least one precipitating factor (Table1). Sleep deprivation even for one night led to considerable increase in myoclonic attacks in 94% of our patients.

Table 1: Frequency rate of the precipitating factors in 32 patients with JME

sleep deprivation	30 cases	94%
photosensitivity	8cases	25%
menses	4 cases	12.5%?
fatigue	19cases	59.4%
stress	26 cases	81.3%
concentration	7 cases	21.9%

Photosensitivity alone or in combination with sleep deprivation was reported in 8 cases (25%). Considerable increase in myoclonic attacks around the menstrual cycle were reported in four cases (29% of the female cases or 12.5% of the whole JME group). Stress causes obvious increase in myoclonic jerks in 26 cases (81.25%). Nineteen cases (59.4%) reported an increase of myoclonic jerks with fatigue. The circadian rhythm influenced JME attacks in 26 cases (81.2%), with most of the myoclonic jerks occurring on awakening from night sleep or a day nap. Six cases (18.75%) which had both myoclonic jerks and GTCS had no definite circadian rhythm influences.

Initial EEG was normal in 37.5% and borderline in 12.5% of patients with JME. In 16 patients (50%), there were epileptic discharges, including focal or generalized spikes, sharp waves, or spike-and-wave activity in the first EEG. After at least three EEGs, the yield of epileptic discharges increased to 27 patients (84.4%). Within this latter group, 7 cases (21.9%) had focal discharges and 20 cases (62.5%) showed generalized epileptic discharges. Positive family history was present in nine patients, as follows: 2 patients with affected parents; 3 patients with one affected sibling; 3 patients with one affected parent and one affected sibling; 1 patient with 2 affected sibling.

DISCUSSION

The clinical characteristics and familial epileptic background of our 32 JME patients is almost similar to other studies worldwide.^{9,10,11,12} The mean age of onset is approximately 10.5 years (range 5 to 16 years) for absence-type seizures, 15 years (range 8 to 26 years) for myoclonic jerks, and 16 years (range 9 to 28 years) for generalized convulsive seizures.⁶ The absence seizures are virtually never preceded by myoclonus or convulsive

seizures. Approximately one-half of JME patients have a family history of one or more of the three seizure types.¹⁰ Myoclonic jerks usually begin before the end of second decade¹² and may be the only manifestation in some patients.^{12,13} Myoclonus is usually unilateral at onset or can be predominantly unilateral.

Epileptic attacks may interfere with daily activities. Absences attacks occurs in 30% of JME cases.^{1,9,12} Most recent studies reveal that the majority of JME cases have GTCS.² This occurs usually on awakening, but may occur during sleep, or randomly during the day.^{10,12,13,14} The circadian symptomatology of JME can be changed as a result of antiepileptic drug therapy.^{14,15} The temporal relationship between JME and GTCS is not persistent. JME was preceded by GCTS in 80% of our cases who had both manifestations. Other studies have reported that JME attacks are usually followed by generalized seizures which occur after several abrupt myoclonic movements.^{9,11,12,16} Several studies describe cases in which there is a constant temporal relation between JME and GTCS.^{11,13} In two of our male cases JME attacks were always followed by GTCS. Most of our patients had circadian influences on JME and if patients used antiepileptic drugs, the influence of the circadian rhythm changed. Other studies have reported that the majority of JME patients have circadian rhythm changes, and antiepileptic drugs can alter this pattern.^{10,18}

Circadian variations may be the result of physiologic changes in neuronal membranes or at the level of the reticular formation; they may also represent effects of systems that are involved in sleep-wake cycles and may predispose to certain situations favoring epileptic discharges. This primary firing (discharge) can be accepted as the cause of short-interval myoclonic movement. If these discharges are circumscribed in their original site, affected persons shows only self-limited myoclonic movement, but the spread of discharges results in GTCS or absence seizure activity.^{13,17}

Precipitating factors are important in initiation and severity of epileptic attacks in most types of epilepsy. Sleep deprivation is one of the most important precipitating factors in patients with JME.¹¹ Reported studies show that photosensitivity is common in JME but the incidence varies widely.^{12,13,18} The cause of this difference can be related to the method and duration of photic stimulation, the effect of antiepileptic medication, and the method of performing EEG.

EEG is the most important paraclinical tool in the diagnostic and therapeutic evaluation of epilepsy, and is usually abnormal in untreated patients.^{1,9,10,12} The EEG

reveals a 4 to 6 Hertz polyspike and wave discharge, which in the younger child with absence seizures may be indistinguishable from that of typical absence epilepsy. In 10 to 15 percent of patients with JME, the initial EEG is normal.^{3,7,16} Repeat EEG should be done in the morning after all-night sleep deprivation if the diagnosis is in doubt.^{7,8,16} Although JME is classified as a generalized epileptic syndrome, focal epileptiform abnormalities on EEG (up to 37 percent of cases in one series) are not uncommon, and some patients may have focal ictal symptomatology.^{7,8} In our studied group, nine cases showed epileptic discharges in the first EEG, but after three EEGs (spaced apart by three to four months) 27 cases showed epileptic discharges. The reported frequency of interictal EEG abnormalities in the literature is 74-88.6%.^{10,12} The reported incidence of photoconvulsive response is variable and depends on the methodology; it has been reported in one-third of patients.^{2,12,14,19,20}

Eye closure is an important precipitating factor both for appearance of myoclonic jerks and for interictal abnormalities. The method adopted for EEG, the sensitivity of the EEG machine, antiepileptic drugs, and condition of the patient at the time of EEG (such as co-existing sleep debt) may explain variation in results in different studies. In our study we used one sensitive EEG machine (Neurofax, Japan), and our method of photic stimulation was flashlight stimulation for three minutes with frequency of 0.5 to 3 Hz.

One of the most important pitfalls in evaluation of JME is delay in diagnosis. An important factor in earlier studies was lack of direct questioning about myoclonic jerks or failure to correctly interpret a history suggestive of myoclonic jerks.^{10,11} Misinterpretation of unilateral myoclonic jerks may result in making a diagnosis of partial epilepsy.^{1,12,21} Absence seizures antedate other types of seizures and these patients may be diagnosed as childhood or juvenile absence epilepsy until JME is revealed by the appearance of myoclonic jerks and GTCS. Focal EEG abnormalities in JME may also be misinterpreted and wrongly ascribed to partial epilepsy.

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