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 seizures which is often associated with Generalized Tonic Clonic Seizure (GTCS) and absence attacks.

Methods: Consecutive patients with probable diagnosis of seizure referred to Vali-e-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 the manifestations, history and EEG findings. Patients who had structural brain lesion were excluded.

Results: 396 epileptic patients including, 32 JME cases (8.1%; 18 males, 14 females) were investigated. Mean age of JME onset and age at the time of diagnosis was 12.4 years and 14.2 years respectively. 27 patients with JME had GTCS and 7 patients had absence epilepsy .Triad of Myoclonia, GTCS and absence was seen in only 4 cases and 2 cases had pure Myoclonia. Myoclonia was predominantly unilateral or at least unilateral at onset in 8 patients (25%). In 28 cases (87.5%) most of attacks occurred on awakening. Sleep deprivation was the most important precipitating factor which was found in 26 cases (81.3%). Characteristic epileptic pattern was found in 71.9% of cases with JME in the first EEG which was promoted to 94% with repeating the EEG. A positive familial history for epilepsy was seen in 25%.

Conclusion: JME is a frequent subtype of generalized epilepsies which is often associated with GTCS and absence. JME patients usually have epileptic pattern in EEG.

Keywords; Juvenile, Myoclonic, Epilepsy, Seizure

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Introduction

JANZ described Juvenile Myoclonic Epilepsy [JME] for the first time in 1957.[1] JME is frequently diagnosed in pediatric epilepsy clinics but is often not recognized by referring clinicians.[2] Myoclonic jerks often occur upon awakening in the morning or during early morning hours which is not 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 a healthy young teenager with one or more of the following seizures.[6] JME is one of the common types of generalized epilepsy and can be recognized by its characteristic clinical feature. 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]. A repeated 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 article represents clinical, EEG and familial characteristics of JME in 32 cases which were visited in two teaching hospitals of Birjand University of Medical Sciences.

Methods

Consecutive patients with convulsive seizures were prospectively evaluated in Vali-e-Asr and Emam Reza hospitals, in Birjand during March 2005- May 2007. These hospitals are the only hospitals whose have neurology division and clinic in southern Khorasan province.

Past medical history and physical exam of all patients were performed by a neurologist. Diagnosis of epilepsy was made based on International League against Epilepsy (ILAE) classification*. Only cases were accepted as JME which was confirmed by two neurologists based on the ILAE definition. The ILAE Criterion for diagnosis of JME includes:

(a) Unequivocal clinical evidence of generalized seizures with myoclonic jerk mainly on awakening. (b) Presence of absence seizure (c) Positive family history of JME, (d) Normal neurologic exam, (e) Characteristic EEG; generalized spikes or multiple spikes and slow wave. Patients who had organic brain insult or their Myoclonia initiated clearly after head trauma had ruled out from our study. Patients with JME were

evaluated based on their age, age at JME onset, gender, family history of JME and lateralization (unilateral or generalized onset) of symptoms. The presence of other seizures, i.e., Generalized Tonic Clonic Seizure (GTCS) and absence, effective drug in controlling seizures and seizure recurrence after termination of therapy were recorded. Other factors that were considered in our study include as follow; Precipitating factors of seizure, circadian distribution and family history of seizures were investigated. All of the patients underwent conventional EEG in the inter-ictal period and brain imaging.

Results

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

Myoclonia has not been as an isolated sign and other types of seizure activities, convulsive or nonconvulsive, have been seen with myoclonia at the same time in 93.7% of the cases with JME. 27 cases (84.4%) of our patients with JME had GTCS. Seven cases with JME (21.9%) had absence seizures followed by myoclonic movements. Two of this later group had some pure absence attacks but more often, absence attacks followed by myoclonic jerks. Four cases (12.5%) of our studied cases had triad of; GTCS, myoclonic jerks and absence. Two cases (6.25%) had pure myoclonia. In all studied cases we could find at least one precipitating factor (table1).

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%	29% of female cases
fatigue	19cases	59.4%	
stress	26 cases	81.3%	
concentration	7 cases	21.9%	

Sleep deprivation even for one night led to considerable increase in myoclonic attacks in 94% of our patients. Photosensitivity alone or in combination with sleep deprivation was reported in 8 cases (25%). Menses: considerable increase in myoclonic attacks were reported in four female cases (29% of the female cases or 12/5% of the whole JME patients).

Stress, causes obvious increase in myoclonic jerks in 26 cases (81.25%). 19 cases (59.4%) reported increasing of myoclonic jerks in fatigue situations. Circadian rhythm had influence in occurrence of JME attacks in 26 cases (81.2%) ; most of the myoclonic jerks have occurred on awakening from sleep night or on awakening from a day nap .Six cases (18.75%) which had both myoclonic jerks and GTCS had no definite circadian rhythm.

The first EEGs were normal and borderline in 37.5% and 12.5% of the patients with JME respectively. 16 patients (50%) had epileptic discharges, focal or generalized spikes, sharp or spike and waves in the first EEG. After at least three EEGs performance, 27 patients (84.4%) showed epileptic discharges. Within this later group, 7cases (21.9%) had focal discharges and 20 cases (62.5%) showed generalized epileptic discharges. Positive family history was present in nine patients; nine studied cases (28.1%) had similar JME attacks in one of their parents or siblings or both. We divided this positive family history group, into four categories.

1-Patients who had one affected parents, including two cases.

2-Patients who had one affected sibling, including three cases.

3-Patients who had one affected parents and one affected sibling Including three cases.

4-Patients who had two affected siblings including one patient.

Discussion

The clinical characteristics and familial epileptic background of our 32 JME patients is almost similar to the other studies worldwide,[9,10,11,12] The mean age of onset of the absence seizures is approximately 10.5 years (range,5to16years), myoclonic jerks at 15 years (range, 8 to 26 years), and the generalized convulsive seizures 16 years (range, 9 to 28 years) .[6] The absence seizures are virtually never preceded by the 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 decade [12] and may be the only manifestation in some patients.[12,13] Myoclonia 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] An Indian study by Mani et al showed lower incidence of absence (5%) in JME cases.[13] Most recent studies revealed that the majority of JME cases have GTCS[2]. Which occurs usually on awaking,[10,12,13,14] but may occur during sleep, or randomly during the day[?]. The circadian rhythm of JME can be changed as a result of antiepileptic drugs therapy.[14,15] The relation between JME and GTCS is not persistent even in a short period of time in one affected person. JME was preceded by GCTS in 80% of our cases who had both of these epileptic manifestations. Other studies reported

that usually JME attacks are followed by generalized seizures which occur after several abrupt myoclonic movements.[9,11,12,16] Several studies describes cases in which there is constant time relation between JME and GTCS,[11,13] in two of our male cases JME attacks always were followed by GTCS. Most of our patients had circadian rhythm in occurrence of JME and If patient used antiepileptic drugs the influence of circadian rhythm had changed. Other studies reported that the majority of JME have circadian rhythm and antiepileptic drugs can change circadian rhythm[10.] Circadian rhythm may be the result of physiologic changes in neuron membrane, reticular formation and effect of systems that involve in sleep and waking circle, that predispose situation for epileptic discharges, this primary firing (discharges) can be accepted as the cause of short time myoclonic movement. If these discharges is circumscribed in its original site, affected person shows only self limited myoclonic movement,[13,17] but if discharges spread, it can cause GTCS or absence seizure.[13] Precipitating factors are important in initiating and severity of epileptic attacks in the most types of epilepsy. Sleep deprivation is 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] The cause of this difference can be related to the method and duration of photic stimulation, effect of administered antiepileptic drug which patient is taking and the method of EEG performance. EEG is the most important paraclinical tool in diagnosis and therapeutic evaluation of epilepsy, i.e. JME 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] Repeating of 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 the 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 finally after taking at least three EEG (the interval between them was at least three to four months) 27 cases showed epileptic discharges. The reported frequency of interictal EEG abnormalities were 74-88.6%.[10,12] The reported incidence of photoconvulsive response is variable and depends on the methodology and has been reported in one-third of patients.[2,12,14,18,19]

Eye closure is an important precipitating factor both for appearance myoclonic jerks and for interictal abnormalities. The method which is adopted for EEG taking, the sensitivity of EEG machine, antiepileptic drugs,

condition of the patient at the day of EEG taking (if he or she have had a sound sleep at the night before) may be the cause of different 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 for the delay in the diagnosis in the earlier studies was missed question about myoclonic jerks or failure to interpret the history which was suggestive of myoclonic jerks.[10,11] Misinterpretation of unilateral myoclonic jerks may result in making a diagnosis of partial epilepsy.[1,12,20] Absence seizures antedate other types of seizure and these patients may be diagnosed as childhood or juvenile absence epilepsy until JME is revealed by the appearance of myoclonic jerks and GTCS*‘. This point was reported out in a study of long-term prognosis of typical childhood absence epilepsy by Wirrell et al[21]. Focal EEG abnormalities in JME may be misinterpreted and diagnosis of partial epilepsy be made.

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ارزیابی بالینی ۳۲ بیمار مبتلا به صرع میوکلونیک جوانان در خراسان جنوبی

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چکیده

سابقه و هدف: صرع میوکلونیک جوانان (JME) از انواع شایع تشنج ژنرالیزه می باشد که معمولاً همراه با تشنج ژنرالیزه تونیک کلونیک (GTCS) وحملات صرع آبسانس می باشد.

روش بررسی: بیمارانی که با تشخیص احتمالی تشنج به بیمارستان های ولی عصر (عج) و امام رضا (ع) خراسان جنوبی از مارس ۲۰۰۵ تا می ۲۰۰۷ ارجاع شده بودند، مورد بررسی قرار گرفته و تشخیص صرع و JME توسط نورولوژیست براساس تظاهرات بالینی، تاریخچه و یافته های الکتروآنسفالوگرافی داده شد. بیمارانی که آسیب نسج مغزی داشتند از مطالعه حذف شدند.

یافته‌ها: ۳۹۶ بیمار صرعی شامل ۳۲ مورد JME (۸/۱٪ شامل ۱۸ مرد و۱۴ زن) بررسی شدند. سن متوسط شروع JME و سن زمان تشخیص به ترتیب ۱۲/۴ و ۱۴/۲ سال بود . ۲۷ بیمار با JME ، حملات GTCS و ۷ بیمار حملات صرعی آبسانس داشتند. ترياد میوکلونی ، GTCS و آبسانس فقط در ۴ مورد از بیماران تحت بررسی دیده شد و ۲ مورد نیز فقط حملات میوکلونی داشتند . در ۸ بیمار (۲۵٪) حملات میوکلونیک عمدتاً یکطرفه یا حداقل درشروع یکطرفه بود . در ۲۸ بیمار (۸۷/۵٪) عمده حملات در زمان بیدارشدن از خواب روی داد. محرومیت از خواب مهمترین فاکتور تحریک کننده بود که در ۲۶ بیمار (۸۱/۳٪) یافت شد. در بررسی الکتروآنسفالوگرافی نمای اختصاصی صرعی در ۷۱/۹٪ بیماران با JME در اولین الکتروآنسفالوگرافی یافت شد که با تکرار الکتروآنسفالوگرافی این طرح اختصاصی در ۹۴٪ بیماران یافت شد . سابقه مثبت فامیلی برای صرع در۲۵٪ بیماران وجود داشت .

نتیجه‌گیری: JME یک زیرگروه شایع از صرع های ژنرالیزه است که معمولاً همراه GTCS و آبسانس دیده می‌شود. بیماران JME غالباً طرح صرعی را در الکتروآنسفالوگرافی نشان می دهند.

واژگان کلیدی: تشنج، صرع، میوکلونیک، جوانان