Epilepsy & Behavior 28 (2013) S87–S90

Contents lists available at SciVerse ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Review

Consensus on diagnosis and management of JME: From founder's observations to current trends

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ARTICLE INFO

Article history:
Received 17 November 2012
Accepted 20 November 2012

Keywords:
JME
Criteria
Management
Consensus

ABSTRACT

An international workshop on juvenile myoclonic epilepsy (JME) was conducted in Avignon, France in May 2011. During that workshop, a group of 45 experts on JME, together with one of the founding fathers of the syndrome of JME ("Janz syndrome"), Prof. Dr. Dieter Janz from Berlin, reached a consensus on diagnostic criteria and management of JME.

The international experts on JME proposed two sets of criteria, which will be helpful for both clinical 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. 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).

For both sets of criteria, patients should have a clear history of myoclonic jerks predominantly occurring after awakening and an EEG with generalized epileptiform discharges supporting a diagnosis of idiopathic generalized epilepsy.

Patients with JME require special management because their epilepsy starts in the vulnerable period of adolescence and, accordingly, they have lifestyle issues that typically increase the likelihood of seizures (sleep deprivation, exposure to stroboscopic flashes in discos, alcohol intake, etc.) with poor adherence to antiepileptic drugs (AEDs).

Results of an inventory of the different clinical management strategies are given.

This article is part of a supplemental special issue entitled *Juvenile Myoclonic Epilepsy: What is it Really?*

1. Introduction

An international workshop on juvenile myoclonic epilepsy (JME) was conducted in Avignon, France in May 2011. During that workshop, a group of 45 experts on JME, together with one of the founding fathers of the syndrome of JME ("Janz syndrome"), Prof. Dr. Dieter Janz from Berlin, reached a consensus on diagnostic criteria and management of JME.

Since the acknowledgment of the official status of JME as a special IGE subsyndrome by the ILAE in 1989 (see Genton et al., this supplement), the syndrome is more and more recognized by clinicians all over the world. It is a topic of increasing interest and relevance, potentially due to easily recognizable clinical characteristics and recent genetic findings (Delgado-Escueta, this supplement). However, this worldwide recognition and increase of studies performed on

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http://dx.doi.org/10.1016/j.yebeh.2012.11.051

different continents have also created confusion about diagnostic criteria, treatment in the different age groups, and lifestyle recommendations. Patients with JME still face suboptimal management.

The purposes of this workshop were as follows:

1. to bring clinicians and scientists, who have been working on different aspects of JME, together to create a better overall understanding of this special IGE subtype;
2. to obtain an international consensus on diagnostic inclusion and exclusion criteria; and
3. to establish an optimal clinical management for JME.

2. Diagnostic criteria

Janz described JME in 1985 (Acta Neurologica Scandinavica) as follows: "Juvenile myoclonic epilepsy is a special syndrome within the primary generalized epilepsies which is characterized clinically by irregular jerks of shoulders and arms (so-called impulsive petit mal) after awakening and electroencephalographically by bilateral-synchronous 4–6/s spike-wave complexes, often in the form of polyspike–waves. The age of onset for this syndrome is predominantly between 12 and 18 years. It mostly starts with isolated jerks which as a rule are soon followed by generalized tonic-clonic seizures (GTCSs). Jerks and GTCSs are provoked by sleep deprivation and predominantly occur after awakening (awakening epilepsy). Sleep deprivation and photostimulation are also very efficient in provoking specific EEG patterns [1]."

Clinicians and scientists from different countries utilize different sets of criteria to diagnose JME, as articulated by the workshop participants (see Table 1 and chapter by Camfield et al. in this supplement). The most controversial issue is whether myoclonic jerks without loss of consciousness and an EEG with generalized epileptiform discharges in patients are obligatory. Some criteria are unequivocal: GTCS, absences, as well as seizures refractory to medication are in keeping with, while provocation by sleep deprivation or visual stimuli are not obligatory, for the diagnosis of JME.

In general, the diagnostic criteria for JME have been broadened over time; some clinicians believe that it is no longer necessary to have myoclonic jerks without loss of consciousness after awakening for diagnosis of JME.

Likewise, there appears to be a loosening of the strict criteria for idiopathic generalized epilepsy (IGE) in general, [2] i.e., abnormal consistent focal EEG features and abnormal MRI results are permissible within limits. In some centers, the workshop organizers found that some clinicians classified patients *without* myoclonic jerks as having JME. A likely explanation could be that the seizures started in such patients during adolescence and had other features that fitted in the syndrome.

Based on the latest insights into the syndrome (see all reviews in this supplement) and discussions with the "father" of JME, Prof. Dr. Dieter Janz, who stressed the importance of jerks without loss of consciousness occurring on or after awakening as the hallmark of JME, the international experts on JME proposed two sets of criteria, which will be helpful for both clinical and scientific (genetic, epidemiological, and imaging studies) purposes (see Table 2).

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).

For both sets of criteria, patients should have a clear history of myoclonic jerks predominantly occurring after awakening and an EEG result with generalized epileptiform discharges supporting a diagnosis of idiopathic generalized epilepsy (see Table 2).

3. Management

Once a diagnosis of JME has been made, clinicians must make management decisions together with the patient. Patients with JME require special management because their epilepsy starts in the vulnerable period of adolescence and, accordingly, they have lifestyle issues that typically increase the likelihood of seizures (sleep deprivation, exposure to stroboscopic flashes in discos, alcohol intake, etc.) with poor adherence to antiepileptic drugs (AEDs). Selection of an appropriate antiepileptic drug (AED) and dosing schedules is essential, as carbamazepine (CBZ) and phenytoin (PHT) may exacerbate seizures, while valproate (VPA) should be avoided in pregnancy.

During this workshop, an inventory of the different clinical management strategies was made. Answers to the following seven questions were as follows:

1. *When does AED treatment start, which factors influence drug choice, and what are the preferred AEDs?*

Table 1
Inventory of the criteria utilized by clinicians and scientists in different countries to come to a diagnosis of JME, as articulated by the participants of the workshop.

Country	Europe									America				Asia
										SW a C America		South America	Canada	Japan
	T	Au	H	Fr	UK	NL	SP	I	D		GENESS	Br	Ca	JP
Myoclonus always?	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Exclusively occurring after awakening?	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No
Jerks without loss of consciousness only?	No	Yes	No	Yes	No	No	Yes	No	Yes	Yes	Yes	No	Yes	No
Onset (early) adolescence	No	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	No	Yes	No	Yes
GTCSs allowed	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Absence seizures allowed	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Provocation necessary	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No
Neurological exam normal	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Cognition abnormal allowed	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	No	No	No	Yes	Yes
Behavior abnormal allowed	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
EEG background normal	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
EEG with gen EA obligatory	Yes	Yes	No	Yes	No	No	Yes	No	No	No	Yes	Yes	No	No
Abnormal MRI allowed	No	No	Yes	Yes	Yes[a]	No	Yes[a]	No	Yes	Yes	Yes	No	No	No
Refractory allowed	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

T= Turkey; Au= Austria; H= Hungary; Fr= France; UK= United Kingdom; NL= The Netherlands; SP= Spain; I= Italy; D= Germany; SW= South West; C= Central; Br= Brasil; Ca= Canada; JP= Japan.
Gen EA: generalized epileptiform abnormalities.
[a] Depends on type and localization of the abnormalities.