

Juvenile myoclonic epilepsy starting in the eighth decade

Vanda Tóth¹, György Rásonyi², András Fogarasi³,
Norbert Kovács¹, Tibor Auer⁴, József Janszky¹

¹ Department of Neurology, University of Pécs, Pécs

² Epilepsy Center, National Institute of Psychiatry and Neurology, Budapest

³ Bethesda Children's Hospital, Budapest

⁴ Department of Neurosurgery, University of Pécs, Pécs, Hungary

Received April 13, 2007 ; Accepted June 14, 2007

ABSTRACT – Juvenile myoclonic epilepsy (JME) typically begins at age 10-17 years. We present two patients, with no previous history of epileptic seizures, in whom JME began after the age of 70. The clinical picture of these patients did not differ from “typical” JME except for the patient's age and age at epilepsy-onset. We suggest that not only symptomatic epilepsy, but also some idiopathic epilepsies, can begin or can be reactivated in elderly people. This may be more evidence that susceptibility to epileptic seizures is increased after 60 years of age.

Key words: juvenile myoclonic epilepsy, idiopathic generalized epilepsy, elderly, age, aggravating effect of AEDs

Idiopathic generalized epilepsy syndromes (IGE) have a typical age-at-onset (Janz and Christian 1957). On the basis of the predominant seizure type and age-at-onset, international classification recognizes four main IGE subsyndromes: childhood absence epilepsy (CAE), juvenile absence epilepsy (JAE), juvenile myoclonic epilepsy (JME), and IGE with tonic-clonic seizures alone (ILAE 1989). Currently, the ILAE classification only recognizes syndromes with onset before adulthood. Three larger studies examined adult-onset, idiopathic generalized epilepsy (IGE) and concluded that adult-onset IGE occurs in 9-28% of all IGE cases (Cutting *et al.* 2001, Marini *et al.* 2003, Nicolson *et al.* 2004), challenging the strict age-dependency of these syndromes. Although these studies included in total 148 patients, only one included a patient who had epilepsy-onset in the eighth decade (Marini *et al.* 2003). In addition, less than 10% of patients in

these studies had experienced onset of epilepsy before the age of 40. In another study, focusing exclusively on the myoclonic form of IGE, Gilliam *et al.* (2000) described 11 cases of adult-onset myoclonic epilepsy: age-at-onset was < 60 in all cases. Searching for late-onset IGE, Loiseau *et al.* (1998) reviewed three population-based databases and a city hospital database, but did not find any IGE beginning after the age of 60. They also reviewed previous reports in the available literature and found only one patient with myoclonic epilepsy beginning after 60. With regard to IGE beginning after 60, Loiseau *et al.* (1998) concluded that “aside from a handful authors no-one has seen such an entity”. In a recent case report, a 74-year-old patient presented with newly diagnosed JME. However, this patient experienced her first seizure at the age of 10, thus, she can not be considered as having adult-onset IGE (Jacob *et al.* 2006).

Correspondence:

Dr. Jozsef Janszky
Department of Neurology,
University of Pecs,
Ret u. 2.,
7623 Pecs
Hungary
Tel.: (+00 36) 72535910
Fax: (+00 36) 72535911
<janszky@index.hu>

Although advanced age is the most common time in life to develop epilepsy (Brodie and Kwan 2005), to our knowledge, only two patients have been reported whose myoclonic form of IGE (JME) began after the age of 60 (Marini *et al.* 2003, Loiseau *et al.* 1998). Here we present two patients in whom JME began after the age of 70 without any previous history or signs of epileptic seizures.

Case reports

Patient 1

The 76-year-old woman was admitted to our in-patient department because of one generalized tonic-clonic seizure. She reported that she had experienced several, symmetrical jerks in her hand before she lost consciousness. Three years earlier, she had experienced jerking for some hours in the morning, which had disappeared without medical intervention. She had had diabetes mellitus treated with insulin since the age of 55. As far as she knew, there was no family history of epilepsy. Neurological examination was normal. Brain MRI revealed mild leukoaraiosis. The EEG showed generalized spike-wave discharges (*figure 1A*). Carotid duplex scan revealed mild atherosclerosis. On the basis of the history of generalized myoclonic jerks, the generalized tonic-clonic seizure and EEG findings, we diagnosed her disorder as juvenile myoclonic epilepsy with onset at the age of 73. After introduction of valproic acid at 900 mg/day, she has had neither myoclonic jerks nor tonic-clonic seizures for the last six months.

Patient 2

The 72-year-old man was admitted to our in-patient department because of two generalized tonic-clonic seizures occurring on the same day. He had a five-year history of essential hypertension and received antihypertensive medication. He had been a smoker for 40 years. His sister and his sister's son suffered from epilepsy with onset during adolescence. Neurological examination was normal. Brain MRI scan showed mild generalized brain atrophy, leukoaraiosis, and multiple lacunar infarcts. A carotid duplex scan revealed mild atherosclerosis. The EEG showed generalized spike-wave discharges (*figure 1B*). Neuropsychological examination revealed mild cognitive impairment. Despite the generalized EEG pattern, on the basis of vascular risk factors and MRI results, the patient was diagnosed with post-stroke focal epilepsy; carbamazepine therapy was initiated. After two weeks of carbamazepine treatment, the patient returned to our outpatient department and reported that he had experienced disabling bilateral jerking after reaching 800 mg/day of carbamazepine. These jerking seizures affected both hands lasted 1–5 minutes but consciousness was not affected. On the basis of the myoclonic and generalized seizures, fam-

ily history of adolescent-onset epilepsy and EEG findings, we reconsidered our first diagnosis and diagnosed his condition as "juvenile" myoclonic epilepsy. Valproic acid (1 000 mg/day) was introduced and the myoclonic jerks have disappeared for the last three months.

Discussion

We present two patients in whom a myoclonic form of IGE started in the eighth decade. The clinical picture of these patients did not differ from the "typical" JME (Janz and Christian 1957, Janz 1997), except for the patients' age and age-at-epilepsy onset. Our cases may be further evidence that susceptibility to epileptic seizures increases beyond the age of 60, and draw attention to the possibility that JME can begin at any age.

Classification of the idiopathic generalized epilepsies (IGE) is based according to two main axes: seizure types and age-at-onset. Seizure types however, overlap in the IGE syndromes (ILAE 1989, Janz 1997). Janz (1997) stated that "the age-at-onset is the strongest single indication of a biological difference between the four major syndromes of IGE". Some epilepsy syndromes even include age in their name. For example, absence epilepsy includes two syndromes differing mainly in their age-at-onset: *juvenile* absence epilepsy (JAE) and *childhood* absence epilepsy (ILAE 1989). Juvenile myoclonic epilepsy typically begins at age 10–17 (Janz and Christian 1957 ILAE 1989, Janz 1997).

Conversely, the incidence of epilepsy shows a U-shape, with a peak before the age of 18, and another in the older age groups, notably after 60 years of age (Hauser 1997). Most epilepsies with onset in older age groups, are thought to be symptomatic, mostly post-stroke or of tumorous origin (Brodie and Kwan 2005). On the other hand, the U-shape of epilepsy incidence may be the result not only of different etiological factors, but also of the higher susceptibility to epileptic seizures in children and elderly people compared with middle-aged patients. For example, mesial temporal lobe epilepsy shows the same age-at-onset distribution as idiopathic epilepsies: one peak around age five and another around age 14 (Janszky *et al.* 2004), suggesting a common susceptibility to epileptic seizures, independent of etiology. An example for reactivation of IGE in elderly people is absence status occurring in elderly people (Bauer *et al.* 2007). These patients had experienced childhood absence seizures, which resolved after puberty and but were then reactivated in older age.

Consequently, we suggest that not only symptomatic epilepsy but also some idiopathic (such as genetic-related) epilepsies can begin or can be reactivated in elderly people. We speculate that the idiopathic nature of epilepsies in the elderly probably remains highly unrecognized and these patients are usually regarded as having focal

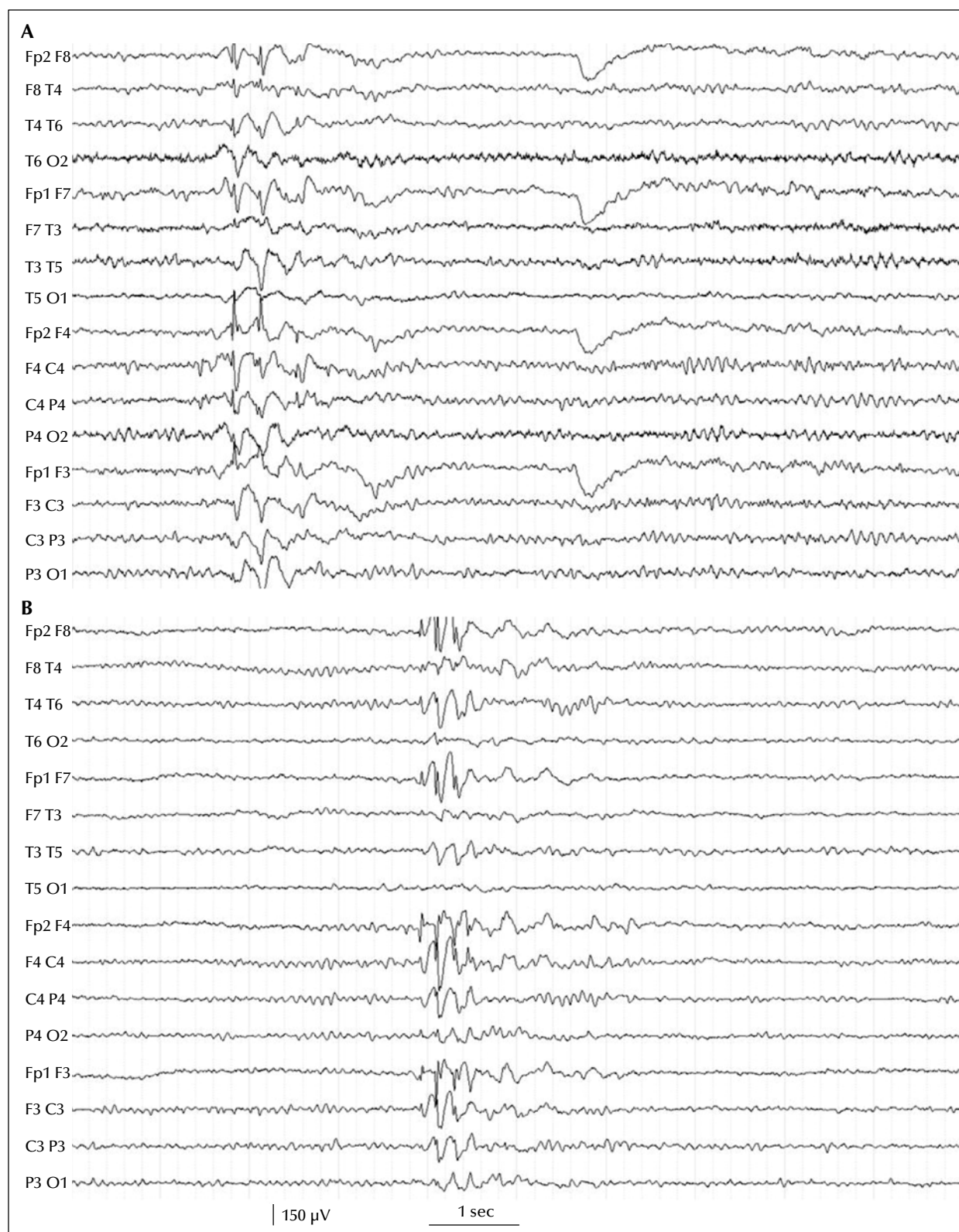


Figure 1. Generalized spike-wave discharges on the routine EEG of patient 1 (**A**) and 2 (**B**) performed during the resting-awake state. The EEG was performed using a digital EEG system (Brain Quick, Micromed, Italy) and presented by longitudinal bipolar montages. Band pass filter: 0.3-70 Hz with a 50 Hz notch filter.

epilepsy of post-stroke origin. The following arguments support this assumption:

(1) *Vascular risk factors or asymptomatic cerebral infarction on MRI, shift the diagnosis towards symptomatic epilepsy*: patient 1 of our study had a long history of diabetes treated with insulin, while patient 2 had chronic hypertension, a 40-year history of smoking and lacunar infarcts on MRI. Furthermore, both patients had mild atherosclerosis in the carotid arteries. These vascular risk factors and presence of silent strokes misled our team in the case of patient 2. He was first diagnosed as having post-stroke epilepsy, considering the fact that stroke is thought to be the one of the major risk factors for epilepsy in the elderly and even asymptomatic cerebral infarction is a supposed risk factor for epilepsy (Brodie and Kwan 2005). After the carbamazepine-induced myoclonic jerks, however, it became clear that patient 2 had IGE of the myoclonic type because carbamazepine has the strongest aggravating potential in JME especially increasing myoclonic jerks (Genton et al. 2000).

(2) *Sleep-deprived EEG is usually not performed* in order to avoid the physical and mental stress it may cause in elderly people. Sleep-deprived EEG is more sensitive to IGE-related epileptiform discharges than routine EEG. The first standard EEG performed, even in a specialized epilepsy center, in patients with JME is misleading in nearly 50% of cases (Genton et al. 1995).

(3) *Elderly people with epilepsy are rarely referred to epilepsy specialist, and elderly patients are rarely asked about the occurrence of myoclonic jerks or family history of epilepsy*. Moreover, a family history of epilepsy often remains inaccurate in elderly people because relatives are often dead or the information about them is incomplete after such a long time.

An alternative explanation for the reactivation or *de novo* appearance of IGE in elderly people is the increasing number of epileptogenic vascular brain lesions occurring during ageing. These can activate generalized epilepsy, and are a supposed triggering mechanism in some IGE appearing after brain trauma (Marosi et al. 1994).

Misdiagnosing IGE as focal symptomatic epilepsy is a common therapeutic failure. Benbadis et al. (2003) analyzed 58 cases of IGE and found that only 29% of patients had been adequately treated with broad-spectrum antiepileptic drugs. In that study, the majority of patients received narrow-spectrum antiepileptics exclusively or in combination with broad-spectrum drugs, which may cause IGE to appear intractable because of lack of efficacy or even the seizure-aggravating potential of narrow-spectrum drugs.

Conclusion

Although most myoclonic epilepsy of IGE appears in adolescence and thus qualify for the term "juvenile" myoclonic epilepsy (ILAE 1989, Janz 1997), clinicians must be

aware that the myoclonic form of IGE can occur in elderly people and is indistinguishable from JME apart from age-at-onset. We hypothesize that IGE in the elderly is under-diagnosed and suggest that systematic studies examining the presence of IGE in the elderly should be performed. We believe that there may be a common misconception in everyday practice that all adults have a focal symptomatic epilepsy, even when the EEG (for example in patient 2) points to an idiopathic generalized epilepsy. Considering our two cases, we emphasize that 1) clinicians should have an open mind about the diagnosis of focal versus idiopathic generalized epilepsy in adulthood; and 2) when the epilepsy syndrome is unclassified, only broad-spectrum AEDs should be used. □

Acknowledgments. This work was supported by grants from the the Hungarian Research Council (ETT 219/2006) and the Hungarian Scientific Research Fund (OTKA T043005 and OTKA F68720). J.J. was supported by the Bolyai Scholarship. A.F. was supported by grant # D 048517 from the Hungarian Scientific Research Fund.

References

- Bauer G, Bauer R, Dobesberger J, et al. Absence status in the elderly as a late complication of idiopathic generalized epilepsies. *Epileptic Disord* 2007; 9: 39-42.
- Benbadis SR, Tatum WO, Gieron M. Idiopathic generalized epilepsy and choice of antiepileptic drugs. *Neurology* 2003; 61: 1793-5.
- Brodie MJ, Kwan P. Epilepsy in elderly people. *BMJ* 2005; 331: 1317-22.
- Cutting S, Lauchheimer A, Barr W, et al. Adult-onset idiopathic generalised epilepsy: clinical and behavioural features. *Epilepsia* 2001; 42: 1395-8.
- Genton P, Gelisse P, Thomas P, et al. Do carbamazepine and phenytoin aggravate juvenile myoclonic epilepsy? *Neurology* 2000; 55: 1106-9.
- Genton P, Gonzales Sanchez MDS, et al. Aspects trompeurs de l'EEG standard dans l'épilepsie myoclonique juvénile: étude rétrospective de 56 cas consécutifs. *Neurophysiol Clin* 1995; 25: 285-90.
- Gilliam F, Steinhoff BJ, Bittermann HJ, et al. Adult myoclonic epilepsy: a distinct syndrome of idiopathic generalized epilepsy. *Neurology* 2000; 55: 1030-3.
- Hauser WA. Incidence and prevalence. In: Engel J, Pedley TA, eds. *Epilepsy: A comprehensive textbook Philadelphia*. Lippincot-Raven Publishers, 1997: 47-57.
- ILAE. Commission on the Classification and Terminology of the International League Against Epilepsy. A revised proposal for the classification of epilepsy and epileptic syndromes. *Epilepsia* 1989; 30: 268-78.
- Jacob S, Martin D, Dajabally YA. Juvenile myoclonic epilepsy in an elderly patient. *Age Ageing* 2006; 35: 194-6.
- Janszky J, Janszky I, Ebner A. Age at onset in mesial temporal lobe epilepsy with a history of febrile seizures. *Neurology* 2004; 63: 1296-8.

Janz D, Christian W. Impulsiv Petit-Mal. *Dtsch Z Nervenheilk* 1957; 176: 346-86.

Janz D. The idiopathic generalized epilepsies of adolescence with childhood and juvenile age of onset. *Epilepsia* 1997; 38: 4-11.

Loiseau J, Crespel A, Picot MC, *et al.* Idiopathic generalized epilepsy of late onset. *Seizure* 1998; 7: 485-7.

Marini C, King MA, Archer JS, *et al.* Idiopathic generalised epilepsy of adult onset: clinical syndromes and genetics. *J Neurol Neurosurg Psychiatry* 2003; 74: 192-6.

Marosi M, Luef G, Schett P, *et al.* The effects of brain lesions on the course of chronic epilepsies. *Epilepsy Res* 1994; 19: 63-9.

Nicolson A, Chadwick DW, Smith F. A comparison of adult onset and "classical" idiopathic generalized epilepsy. *J Neurol Neurosurg Psychiatry* 2004; 75: 72-4.