

Focal epilepsy recruiting a generalised network of juvenile myoclonic epilepsy: a case report

Myo Khaing^{1,2}, Kheng-Seang Lim¹, Chong-Tin Tan¹

¹ Division of Neurology, Department of Medicine, Faculty of Medicine, University of Malaya, Malaysia

² Department of Medicine, University of Medicine, Mandalay, Myanmar

Received May 19, 2014; Accepted July 4, 2014

ABSTRACT – We report a patient with juvenile myoclonic epilepsy who subsequently developed temporal lobe epilepsy, which gradually became clinically dominant. Video telemetry revealed both myoclonic seizures and temporal lobe seizures. The temporal lobe seizures were accompanied by a focal recruiting rhythm with rapid generalisation on EEG, in which the ictal EEG pattern during the secondary generalised phase was morphologically similar to the ictal pattern during myoclonic seizures. The secondary generalised seizures of the focal epilepsy responded to sodium valproate, similar to the myoclonic epilepsy. In this rare case of coexistent Juvenile Myoclonic Epilepsy and Temporal lobe epilepsy, the possibility of focal epilepsy recruiting a generalised epileptic network was proposed and discussed.

Key words: epileptic network, juvenile myoclonic epilepsy, focal epilepsy, electroencephalography

Juvenile myoclonic epilepsy (JME) may coexist with focal epilepsy. However, the coexistence of these two types of epilepsy has been rarely reported (Diehl *et al.*, 1998, Koutroumanidis *et al.*, 1999, Usui *et al.*, 2005, Jeha *et al.*, 2006). One suggested reason for this rarity is the failure to recognise and correctly diagnose one of the two epilepsies (Koutroumanidis *et al.*, 1999). However, there are no reports of a shared epileptic network between coexistent focal epilepsy and JME.

The coexistence of generalised and focal epilepsies in the same patient might be explained by epileptic net-

work, which is a functionally and anatomically connected set of cortical and subcortical brain regions where activity in any one part affects the activity in all others. Generalised epileptic seizures are believed to originate at some point and rapidly engage within bilaterally distributed networks (Berg *et al.*, 2010).

Focal epileptic seizures are conceptualised to originate within networks limited to one hemisphere (Berg *et al.*, 2010). They may be discretely localised or more widely distributed. They may originate in subcortical structures. For each seizure type, ictal onset is

Correspondence:

Kheng-Seang Lim
Neurology Laboratory,
6th Floor, Menara Selatan,
University Malaya Medical Centre,
59100 Kuala Lumpur,
Malaysia
<kslimum@gmail.com>

consistent, from one seizure to another, with preferential propagation patterns that can involve the contralateral hemisphere. In some cases, however, there is more than one network and more than one seizure type and each individual seizure type has a consistent site of onset.

This case report describes a patient with pre-existing JME who developed focal epilepsy which recruited the existing network of generalised epilepsy.

Case study

Juvenile myoclonic epilepsy

A 33-year-old, right-handed Malaysian lady was diagnosed with juvenile myoclonic epilepsy at the age of 14 years, and presented with early-morning myoclonic jerks of either upper or lower limbs with a frequency of one to two per week. The jerks were occasionally accompanied with generalised tonic-clonic seizures. Each generalised tonic-clonic seizure lasted approximately two minutes, with postictal drowsiness. Most of the attacks were precipitated by sleep deprivation and fatigue. She did not have a history of febrile seizures during childhood or a family history of seizures. The frequency of seizures was reduced with the introduction of sodium valproate.

Focal epilepsy

When she was 18 years old, the seizures were found to be more frequent, especially during perimenstrual periods, and occurred mostly at night. The EEG recorded at the age of 22 revealed several episodes

of frontally-predominant generalised spikes, sharp waves, or polyspike-wave complexes. In the past year, she started to experience ascending epigastric aura and fear, followed by generalised tonic-clonic seizures. A diagnosis of temporal lobe epilepsy was made based on the semiology, despite having generalised EEG discharges. She did not have symptoms suggestive of autoimmune disorders or any vascular risk factors. She could not tolerate carbamazepine, failed to response to an optimal dose of topiramate, and was subsequently treated with a combination of lamotrigine and low-dose sodium valproate. Her seizures remained refractory with a frequency of 4-6 seizures a month. Brain MRI performed in 2012 revealed only left basal frontal gliosis, without any temporal lobe abnormalities (*figure 1*). An epilepsy pre-surgical assessment was thus arranged.

Video telemetry

The video-EEG monitoring performed in 2013 showed frequent frontally predominant generalised polyspike-wave complexes, associated with brief myoclonic jerks at times (*figure 2A*). She had five focal seizures with posterior temporal ictal onset; three right-sided and two left-sided. All focal recruiting discharges evolved into a generalised tonic-clonic seizure (*figure 2B*). The patient had expression of fear during the focal discharges. One subclinical seizure was recorded with left posterior temporal ictal onset. A diagnosis of coexistent JME and temporal lobe epilepsy was made. The finding of left basal frontal gliosis based on the brain MRI was viewed as an incidental finding and unlikely to be the epileptogenic lesion, according to the members of the comprehensive epilepsy program.

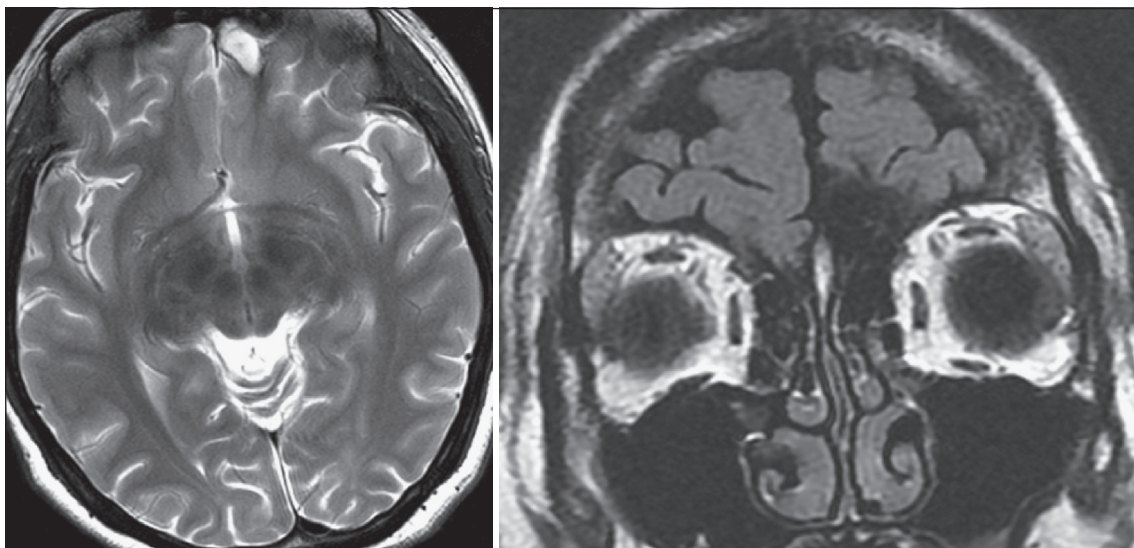


Figure 1. Axial T2-weighted and coronal T2-weighted FLAIR MRI sequences show left orbital frontal gliosis, as circled.

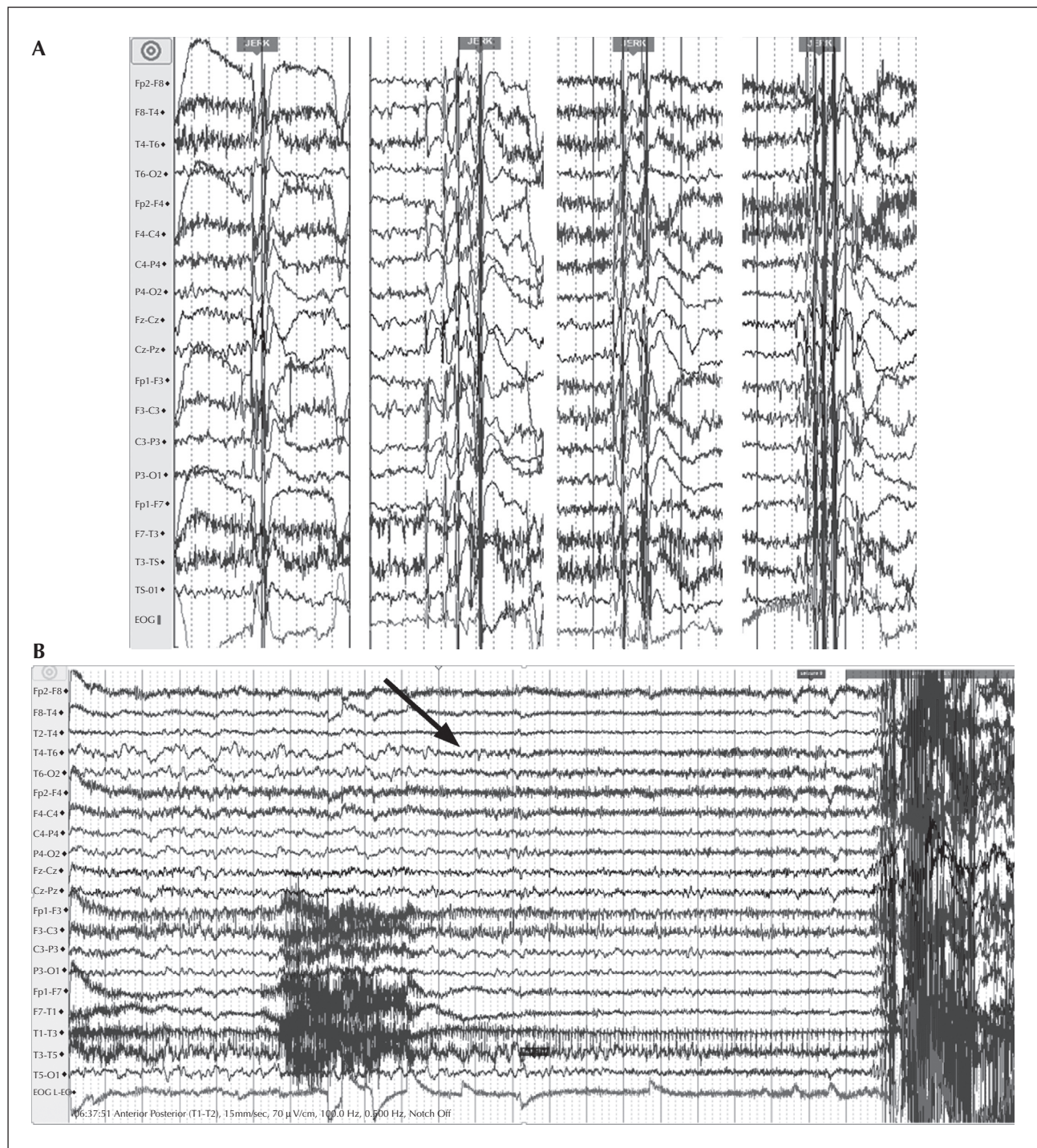


Figure 2. (A) EEG showed frequent 4-6-Hz generalised polyspike-wave discharges associated with myoclonic jerks clinically. (B) EEG (70 μ V/cm and 15 mm/sec), showed a right posterior temporal (T6) fast-recruiting rhythm (as circled) followed by 6-Hz generalised polyspike-wave discharges associated with myoclonic jerks clinically. (C) (average montage) The T6 recruiting rhythm was demonstrated on an average montage.

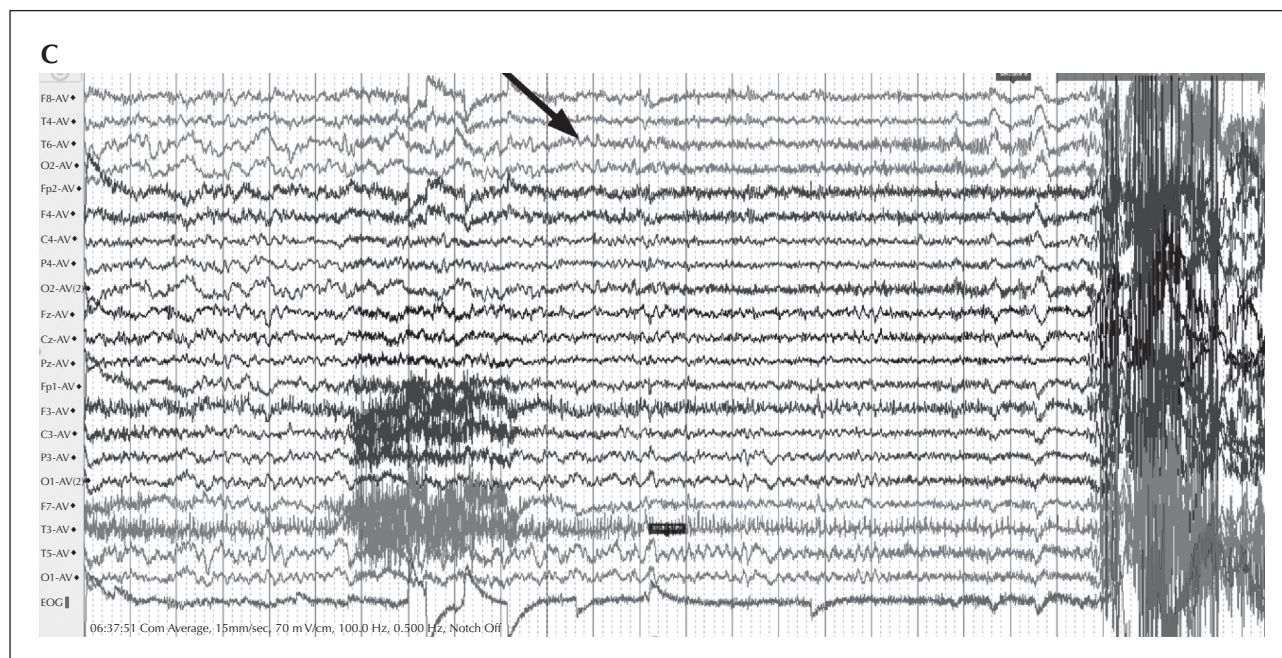


Figure 2. (Continued)

Follow-up

Sodium valproate was titrated up to 1,200 mg per day, resulting in resolution of the secondary generalisation of her focal seizures.

Discussion

The juvenile onset of the early-morning myoclonic jerks with or without generalised tonic-clonic seizures precipitated by sleep deprivation and fatigue, the presence of generalised polyspike-wave discharges on EEG, and response to sodium valproate are consistent with the diagnosis of JME. The patient had a second epilepsy syndrome, which was different in presentation from the myoclonic epilepsy and refractory to topiramate and lamotrigine. The second epilepsy syndrome was likely to be focal epilepsy, as supported by ascending epigastric aura and fear, a catamenial nature, occurrence at night, and focal ictal onset based on the video telemetry.

The coexistence of JME and TLE has been rarely reported. A 0.2% incidence of coexistent focal and primary generalised epilepsy was reported in a group of patients hospitalised at the Cleveland Clinic Epilepsy Monitoring Unit (Jeha *et al.*, 2006). MRI of these patients showed hippocampal atrophy in all patients and hippocampal dysplasia in three patients. Usui *et al.* studied 26 patients with JME who had seizures

recorded during video-EEG monitoring and found that 14 patients (54%) had focal semiological or EEG features, or both (Usui *et al.*, 2005). Two patients (7.7%) had both TLE and JME in their study. Lie and Holmes (2012) described late-onset temporal lobe epilepsy in a patient with JME. In their report, the age at onset of JME was 14. Twenty-nine years later, the patient had new episodes of “jumbled” speech and prolonged staring. An EEG showed novel, bilateral independent temporal interictal spikes, preceding bursts of generalised discharges. Brain MRI showed right hippocampal sclerosis.

Documentation of both generalised and focal seizures during the same video-EEG telemetry in this patient was not described in the previous case report (Lie and Holmes, 2012). This observation is important for direct comparison between the epileptic networks of both focal and generalised epilepsy. There were two distinct epileptic networks as evidenced by the presence of two different ictal EEG activities, *i.e.* generalised polyspike-wave complexes and focal ictal recruiting rhythms. However, there was evidence supporting a shared network between the two seizure types, as follows: (1) the EEG pattern during the secondary generalised phase of the focal seizures was similar to the polyspike-wave discharges observed during the myoclonic seizures, and (2) the secondary generalised seizures responded to sodium valproate, similar to the myoclonic seizures, suggesting that the secondary generalised component of the focal epilepsy

involved the same network as that of the myoclonic epilepsy. Therefore, we postulated that the focal seizures recruited the generalised network of JME in the patient with coexistent JME and focal epilepsy.

The connectivity between the myoclonic epilepsy and focal epilepsy in this patient may be due to the involvement of the temporal structures in the epileptic circuits of JME. In addition, in the absence of other possible acquired aetiologies, the focal epilepsy could be a result of secondary epileptogenesis due to chronic JME. In a PET study of JME patients, serotonin receptor binding was found to decrease locally at the hippocampus suggesting hippocampal neuronal loss or dysfunction (Meschaks *et al.*, 2005). Decreased cortical thickness in temporal regions in JME patients (Tae *et al.*, 2008) and hippocampal metabolic dysfunction using a 3D multivoxel spectroscopy study (Ristic *et al.*, 2011) in patients with JME were reported. Using source analysis of dense-array EEG-recorded epileptiform discharges, localised involvement of basal and mesial temporal lobe structures, in addition to frontal regions, was identified in five of ten patients with JME (Holmes *et al.*, 2010).

Response of the secondary generalised component of the focal epilepsy, but not the focal seizures, to sodium valproate suggests that (1) a different epileptic network responds to antiepileptic drug differently, and (2) the secondary generalised component of focal epilepsy can be treated successfully, even though the initial focal activity is refractory to treatment.

In this rare case of coexistent JME and TLE, the possibility of focal epilepsy recruiting a generalised epileptic network was proposed and discussed. The benefit of treating the generalised networks separately was demonstrated. Future studies using EEG-fMRI (functional MRI) or magnetoencephalography (MEG) on such patients may help to confirm our hypothesis of the potential relationship between the epileptic networks of generalised and focal epilepsies. □

Acknowledgements and disclosures.

The work was not supported by any source of funding. The authors have no conflicts of interests to declare.

References

- Berg AT, Berkovic SF, Brodie MJ, *et al.* Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005-2009. *Epilepsia* 2010; 51: 676-85.
- Diehl B, Wyllie E, Rothner AD, Bingaman W. Worsening seizures after surgery for focal epilepsy due to emergence of primary generalized epilepsy. *Neurology* 1998; 51: 1178-80.
- Holmes MD, Quiring J, Tucker DM. Evidence that juvenile myoclonic epilepsy is a disorder of frontotemporal corticothalamic networks. *Neuroimage* 2010; 49: 80-93.
- Jeha LE, Morris HH, Burgess RC. Coexistence of focal and idiopathic generalized epilepsy in the same patient population. *Seizure* 2006; 15: 28-34.
- Koutroumanidis M, Hennessy MJ, Elwes RD, Binnie CD, Polkey CE. Coexistence of temporal lobe and idiopathic generalized epilepsies. *Neurology* 1999; 53: 490-5.
- Lie OV, Holmes MD. Late-onset temporal lobe epilepsy in a patient with juvenile myoclonic epilepsy. *Epileptic Disord* 2012; 14: 190-4. doi: 10.1684/epd.2012.0500.
- Meschaks A, Lindstrom P, Halldin C, Farde L, Savic I. Regional reductions in serotonin 1A receptor binding in juvenile myoclonic epilepsy. *Arch Neurol* 2005; 62: 946-50.
- Ristic AJ, Ostojic J, Kozic D, *et al.* Hippocampal metabolic dysfunction in juvenile myoclonic epilepsy: 3D multivoxel spectroscopy study. *J Neurol Sci* 2011; 305: 139-42.
- Tae WS, Kim SH, Joo EY, *et al.* Cortical thickness abnormality in juvenile myoclonic epilepsy. *J Neurol* 2008; 255: 561-6.
- Usui N, Kotagal P, Matsumoto R, Kellinghaus C, Luders HO. Focal semiologic and electroencephalographic features in patients with juvenile myoclonic epilepsy. *Epilepsia* 2005; 46: 1668-76.