SHORT COMMUNICATION

Focal-onset myoclonic seizures and secondary bilateral synchrony

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Introduction

Secondary bilateral synchrony (SBS) is characterized by bilateral synchronous discharges on scalp EEG that can be shown to arise from a unilateral cortical focus (Tükel and Jasper, 1952). The identification of SBS, despite the appearance of generalized epileptiform discharges, is critical in the evaluation of focal epilepsy, as it may allow for potentially curative treatment with focal resective surgery.

Subsets of seizures that were traditionally categorized as generalized can be focal in origin. Absences (Farwell and Stuntz, 1984; Yamanouchi et al., 1992; Millan et al., 2001) and epileptic spasms (Chugani et al., 1992; Akiyama et al., 2005; Ramachandranair et al., 2008) with focal onset have been reported. Myoclonic seizures, a hallmark of generalized epilepsy syndromes, can have focal onset. However, to our knowledge, there has been only one published report of myoclonic seizures with suggested SBS (Kobayashi et al., 2000).

We report a child with myoclonic seizures, epileptic spasms and generalized epileptiform discharges resembling myoclonic–astatic epilepsy, in which intracranial video EEG (IVEEG) confirmed SBS.

Case report

An eight-year-old right-handed boy presented with brief staring spells at one year of age. Generalized tonic–clonic
and epileptic spasms (Fig. 1) with right-side dominant arm approximately 20 seizures daily with head drops or limb tigation for surgical treatment. At this time he was having difficulty in maintaining the ketogenic diet required reinves-
less intensity. At 7 years 3 months, continuing seizures and seizures resolved, seizures with limb jerking remained with at 4 years 9 months. Although generalized tonic—clonic gyri. A 1.5-T esla MRI was reported to be nor-
mal. Scalp video EEG detected 12 dipoles in the left superior and middle lobe.

The patient underwent left frontal lobectomy including the regions of the MEG dipole cluster and the MRI lesion. Direct cortical stimulation for functional language mapping demonstrated no language function in the left frontal lobe.

Figure 1 Ictal scalp EEGs at 7 years 3 months. A. Myoclonic seizure. There is a brief burst of bifrontal and then generalized polyspike-and-waves accompanied with repetitive, brief deltoid muscle contractions, more prominently on the right. B. Epileptic spasm. There are generalized polyspikes immediately followed by diffuse high-amplitude 1—1.5 Hz delta waves and then bifrontally dominant 9—10 Hz activity lasting for 1.5 s. There is a right deltoid muscle contraction lasting for 0.7 s.

seizures and seizures with bilateral arm jerking started after two years of age. Four anti-epileptic drugs failed to suppress his seizures.

Pre-natal, peri-natal and past medical history were unre-
morable. Development was normal. Family history was only positive in his cousin with epilepsy.

The child was referred to The Hospital for Sick Children at four years of age. Neurological examination was unre-
markable. Scalp video EEG recorded six myoclonic seizures involving bilateral arms with generalized polyspike-and-waves. The background activity during wakefulness and sleep features were normal. Bilateral synchronous, frontal spike-and-waves with left hemispheric predominance and generalized polyspike-and-waves were intermittently seen (Supplementary Fig. 1). Magnetoencephalography (MEG) at 4 years 9 months demonstrated 23 equivalent cur-
rent dipoles on the left and five on the right, with a cluster of 12 dipoles in the left superior and middle frontal gyri. A 1.5-Tesla MRI was reported to be normal.

It was decided to treat the patient initially with the ketogenic diet based on the resemblance of the semiology of his epilepsy to that of myoclonic—astatic epilepsy. A medium-chain-triglyceride ketogenic diet was initiated at 4 years 9 months. Although generalized tonic—clonic seizures resolved, seizures with limb jerking remained with less intensity. At 7 years 3 months, continuing seizures and difficulty in maintaining the ketogenic diet required reinves-
tigation for surgical treatment. At this time he was having approximately 20 seizures daily with head drops or limb jerking.

The second scalp video EEG captured myoclonic seizures and epileptic spasms (Fig. 1) with right-side dominant arm jerking. During the interictal period, bilateral synchronous, frontal spike-and-waves and generalized polyspike-and-
waves were seen. Mu rhythm was consistently absent in the left hemisphere. Coherence-phase analysis for 50 interictal generalized polyspike-and-waves demonstrated left-sided lead in 23 (46%), right-sided lead in 5 (10%), and no evidence of lateralization in 22 (44%), suggesting SBS with left hemisphere lead by up to 27.3 ms (Fig. 2).

The second MEG at 7 years 3 months continued to show a left-sided predominance demonstrating 64 dipoles on the left and 13 on the right. Sixty dipoles clustered within the left superior and middle frontal gyri, and spread to the motor cortex (Fig. 3A). A 3-Tesla MRI demonstrated an area with subtle increased T1 signal in the cortex of the left superior frontal gyrus with subtle blurring of the grey-white matter junction (Supplementary Fig. 2). This was thought to be suspicious for focal cortical dysplasia. Neuropsychological assessment at 8 years showed an average IQ profile and attention below the second percentile for age. Vocabulary was described as poor but within normal limits. Functional MRI for language was not feasible due to young age.

Due to the focal MEG findings and the subtle lesion on MRI, it was decided to proceed with IVEEG monitoring. A subdu-
ral grid, a subdural strip, a depth electrode were placed over/into the left hemisphere and two subdural strips over the right hemisphere (Fig. 3B). IVEEG was recorded for 96 h at 1 kHz sampling rate (Harmonie system, Stellate, Montreal, PQ, Canada).

This IVEEG captured 45 myoclonic seizures and 8 epilep-
tic spasms with asymmetric tonic posturing (extension of the right arm and leg; flexion of the left arm). Ictal EEGs of myoclonic seizures showed bilateral synchronous polyspike-and-waves with left frontal leading by up to 35 ms (Fig. 3C—E). The topographic movie of high-frequency oscillations (HFOs) at ≥80 Hz during the myoclonic seizure demonstrated initial increase in HFO amplitude in the left frontal lobe with subsequent spread to the right hemi-
sphere (Video 1 and Fig. 3F). Ictal EEGs of epileptic spasms showed similar polyspike-and-waves with left frontal leading followed by low-amplitude fast waves (Supplementary Fig. 3A—C). The topographic movie of HFOs during the epileptic spasm also demonstrated seizure onset in the left frontal lobe followed by spread to the right hemisphere (Video 2 and Supplementary Fig. 3D). The methodology of these topographic movies is described elsewhere (Akiyama et al., 2011). There were frequent interictal polyspike-and-waves over bilateral frontal lobes synchronously or independently with left-sided predominance, including the regions with the MEG dipole cluster and the MRI lesion. Direct cortical stimulation for functional language mapping demonstrated no language function in the left frontal lobe.

Discussion

We demonstrated that both myoclonic seizures and epileptic spasms in this patient were of focal onset, originating from the left frontal lobe with extremely rapid secondary generalization by iEEG. This is a confirmed case of focal epilepsy with SBS, resembling myoclonic–astatic epilepsy, treated with focal resective surgery.

There has been limited published data on SBS in myoclonic seizures, in contrast to increasing evidence that another traditionally generalized seizure type, i.e. epileptic spasms, may have a focal onset (Chugani et al., 1992; Akiyama et al., 2005; Ramachandrannair et al., 2008). Kobayashi et al. demonstrated myoclonic seizures caused by probable SBS in a patient with myoclonic seizures and complex partial seizures (Kobayashi et al., 2000). However, to our knowledge, there have been no reports of myoclonic seizures with SBS confirmed directly by intracranial EEG.

In this child, the topographic movie of a myoclonic seizure demonstrated that HFOs at $\geq 80$ Hz started in the left inferior frontal gyrus then spread rapidly within the left frontal lobe and towards the right hemisphere. In the topographic movie of an epileptic spasm, HFOs started in the left middle to superior frontal gyri. Analysis of HFOs at 200–300 Hz demonstrated an almost identical pattern. We previously reported the utility of the ictal HFO movie for Jacksonian seizures (Akiyama et al., 2011). HFOs at seizure onset have been known to indicate the seizure onset zone (Allen et al., 1992; Fisher et al., 1992; Traub et al., 2001; Jirsch et al., 2006). Moreover, the propagation pattern of HFOs during seizures is valuable in the estimation of the location and extent of the epileptic network (Ochi et al., 2007).

MEG is helpful to detect focal onset in generalized discharges with SBS (Tanaka et al., 2005; Chang et al., 2009). MEG has many advantages over scalp EEG, such as high spatial resolution, less conductivity issues and increased sensitivity for discharges from smaller area (Oishi et al., 2002). MEG is able to detect focal, leading and consistent discharges before rapid spread to extensive cortical regions and thereby demonstrate SBS in subsets of patients with generalized epileptiform discharges on scalp EEG.

Coherence-phase analysis is a helpful tool to estimate interhemispheric time differences suggestive of SBS. This method was originally applied by Gotman (1981) and developed further by Kobayashi et al., using the two-dimensional autoregressive model, to allow for analysis of spike-and-wave epochs of much shorter duration. Interhemispheric time differences of 9 ms or more, with a consistent hemisphere lead, were considered to indicate SBS (Kobayashi...
Figure 3  Intracranial ictal EEG of a myoclonic seizure. A. Subdural grid electrode (109 contacts, magenta) over the left frontal, parietal and temporal lobes, subdural strip electrode (LF1-4, LF1 deepest, magenta) over the MRI lesion (pink), depth electrode (D1-4, D1 deepest, light blue) into the cluster of MEG dipoles (green), subdural strip electrodes (RC1-4, RF1-4, purple) over the right hemisphere, coregistered to 3-D brain MRI. B. Photograph of the left hemisphere with subdural grid electrode, subdural strip electrode, and depth electrode (D1-4). C. Ictal intracranial raw EEG. There are three repetitive spike-and-waves, which were focal at onset and subsequently became wide-spread and accompanied by brief muscle activity on bilateral deltoid electromyograms (EMG). The blue bar at the bottom indicates the section demonstrated in the panel D and E. D. Temporally expanded raw EEG. The earliest spike peak in the left inferior frontal lobe (highlighted in red) preceded that in the right by 35 ms. E. Temporally expanded EEG high-pass filtered at 80 Hz. The earliest onset of high-frequency oscillations (HFOs) were seen in the left inferior frontal lobe (highlighted in red), which preceded HFOs in the right by 35 ms. F. Serial topographic maps of the amplitude of ictal HFOs at ≥80 Hz calculated by Hilbert transform (detailed explanation available in Akiyama et al., 2011). The time point zero (t = 0 ms) corresponds to the onset of HFOs over the left hemisphere (left vertical line in the panel E). There is initial increase in amplitude at the left inferior frontal lobe with subsequent spread to the left superior frontal lobe including the Rolandic region and the right hemisphere. The onset time of EMG activity is 78 ms.
et al., 1992). In our previously reported case of a child with epileptic spasms secondary to a deep mesial temporal tumor, coherence-phase analysis demonstrated a consistent ipsilateral lead, with a mean time difference of 17 ms, even though the ictal EEG discharges were predominant in the contralateral hemisphere (Otsubo et al., 1999). In their case, Kobayashi et al. documented interhemispheric time differences of at most 27.4 ms during myoclonic seizures (Kobayashi et al., 2000). The case reported here demonstrated predominantly left frontal lead of up to 27.3 ms in the interictal discharges.

Considering the pathophysiology of myoclonic seizures and epileptic spasms in this child, the initial spike-wave morphology, HFOs arising from the left frontal lobe and spreading towards the Rolandic region, and latency to the onset of electromyogram activities were identical. The HFOs during epileptic spasms lasted longer within Rolandic and middle–superior frontal regions than those during myoclonic seizures. Nariai et al. found the manifestation of the ictal motor symptoms in epileptic spasms correlated with the amplitude of HFOs at 80—200 Hz in the Rolandic region (Nariai et al., 2011). The topographic movie of HFOs demonstrated the different distribution of the symptomatogenic zone between myoclonic seizures and epileptic spasms in this patient.

Electroclinically, this child showed right-side dominant seizure semiology and epileptiform discharges with left-hemispheric predominance, although these lateralizing signs were quite subtle. Consistent absence of Mu rhythm was confirmed in the left hemisphere. The scrutiny and confirmation of such subtle focal electroclinical signs are essential to the resective surgery for focal epilepsy.

Conclusion

This case demonstrates that subsets of myoclonic seizures with bilateral synchronous discharges on scalp EEG can be focal in origin. IVEEG and ictal HFO analysis confirmed seizure onset in the left frontal lobe. When there is a clinical suspicion of SBS, even in myoclonic seizures with bilaterally synchronous epileptiform discharges, the possibility of focal onset needs to be thoroughly investigated as a subset of these patients will benefit from focal resective surgery.

Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.eplepsyres.2011.02.006.

References


