

Bilaterally independent epileptic spasms in a case of Aicardi syndrome

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ABSTRACT – A girl with Aicardi syndrome was observed to have two distinct types of asymmetric epileptic spasms, as detected by ictal video-EEG recording at three months of age. When the two types of spasm concurred, they showed no mutual interactions based on either clinical or EEG aspects. This observation does not support the hypothesis that the brainstem always plays an initiating role in generating spasms. [*Published with video sequences*]

Key words: Aicardi syndrome, ictal video-EEG recording, infantile spasms

The generation of epileptic spasms (ES), or infantile spasms, is traditionally considered to involve the brain subcortical structures, particularly the brainstem, as well as pathological interaction with the cortex (Dulac and Tuxhorn, 2005). Although a recent influx of reports on successful treatment of ES by cortical resection indicates that some ES originate from the cortex (Asano *et al.*, 2005), the question of whether the brainstem also affects the occurrence of ES in such situations remains unanswered. Data that may help answer this question are provided by the present case of Aicardi syndrome, exhibiting two different types of ES.

Case report

The female patient was born at 41 weeks gestation with a weight of 3468 g without asphyxia. There was no abnormality in her family history. Ventricular dilatation was suggested by foetal ultrasonography at six months of gestation. She started to have convulsive seizures on the fourth day of life, and her seizures changed into ES at around two months of age. The infant was admitted to Okayama University Hospital at three months of age; neurological examinations showed generalised hypotonia with no head control and no visual following. She did not smile. A fundoscopic examination



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revealed bilateral chorioretinal lacunae. MRI demonstrated complete agenesis of the corpus callosum along with cortical dysplasia of the bilateral frontal lobes and a cystic lesion in the third ventricle (*figure 1*). Thus, the diagnosis of Aicardi syndrome was made (Ohtsuka *et al.*, 1993). She had no defects in either the vertebrae or the spinal cord. No abnormality was detected by a battery of examinations, including blood biochemistry, blood gas analysis, cerebrospinal fluid, plasma amino acid analysis, urinary organic acid analysis, abdominal ultrasonography, or cardiac ultrasonography.

The infant was found to have two distinct types of ES which occurred in series but independently, as well as hypsarrhythmia with bilaterally independent periodicity on EEG. Analysis of part of the ictal EEG data has been published previously (Kobayashi *et al.*, 2004). One type of spasm (hereafter denoted as type A), characterised by downward forceful extension of the right arm, extension of the right leg, mild extension of the left leg and foot, and flexion of the left arm, was associated with left-hemispheric high-voltage slow waves (HVS) on EEG (*figure 2A*; see *video sequence 1*). The other type of spasm (denoted as type B), characterised by upward extension of the bilateral upper extremities and flexion of the lower ones with rightward deviation, was associated with right-hemispheric HVS (*figure 2B*; see *video sequence 2*).

The patient experienced 5 to 10 clusters of ES per day, with the total number of spasms per day ranging from around 100 to 300. We recorded ictal video-EEG of two different types of spasm occurring simultaneously, and observed that each type maintained an independent pace and ictal symptomatology. The two types of ES

showed no mutual interaction based on either clinical or EEG aspects (*figure 3*; see *video sequence 3*). Thirty percent of the patient's seizures were type A spasms, 60% were type B spasms, and 10% consisted of both types simultaneously. No focal seizures were observed and we found no focal discharges at the onset of series of ES.

Regarding treatment of ES, the patient did not respond to synthetic ACTH therapy, ketogenic diet, or thyrotropin-releasing hormone (TRH), or to various antiepileptic drugs, including sodium valproate, clobazepam, zonisamide, nitrazepam, lorazepam, and pyridoxal phosphate.

The patient exhibited rigidospastic tetraplegia with severe sclerosis but no signs of development such as head control or visual following, as of her last follow-up visit at nine years of age. The two types of ES persist, although the motor symptoms of spasms have become milder and the frequency of spasms has decreased to several clusters per week. Isolated tonic spasms are also sporadically observed.

Discussion

It has been demonstrated that ES can have a focal cortical onset, based on the reports of successful suppression of ES by cortical resection in many patients with brain tumours, cortical malformation, or tuberous sclerosis (Mimaki *et al.*, 1983; Asano *et al.*, 2005), as well as the detection of ictal high-frequency oscillations through cortical electrodes (Akiyama *et al.*, 2005; RamachandranNair *et al.*, 2008). It is also known that asymmetric behavioural manifestations of ES,

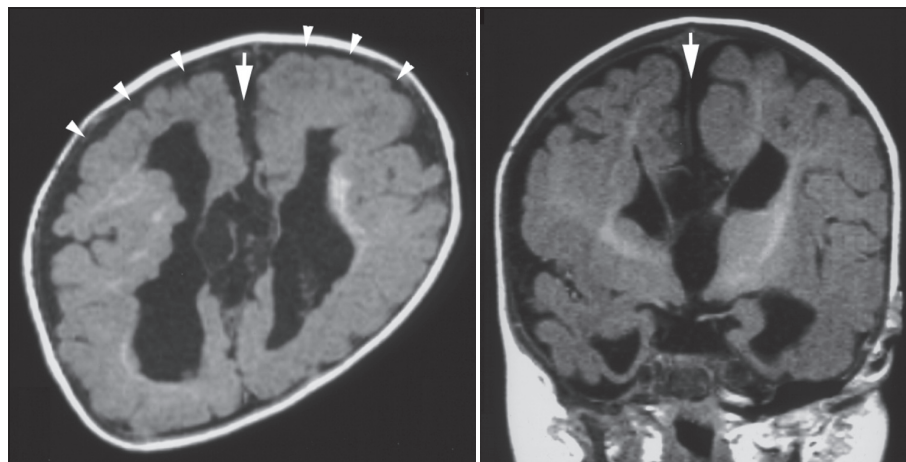


Figure 1. MRI of Aicardi syndrome. MRI (magnetization prepared rapid gradient-echo, MP-RAGE) shows agenesis of the corpus callosum (arrow) and associated cortical malformation in the bilateral frontal lobes (arrowhead).

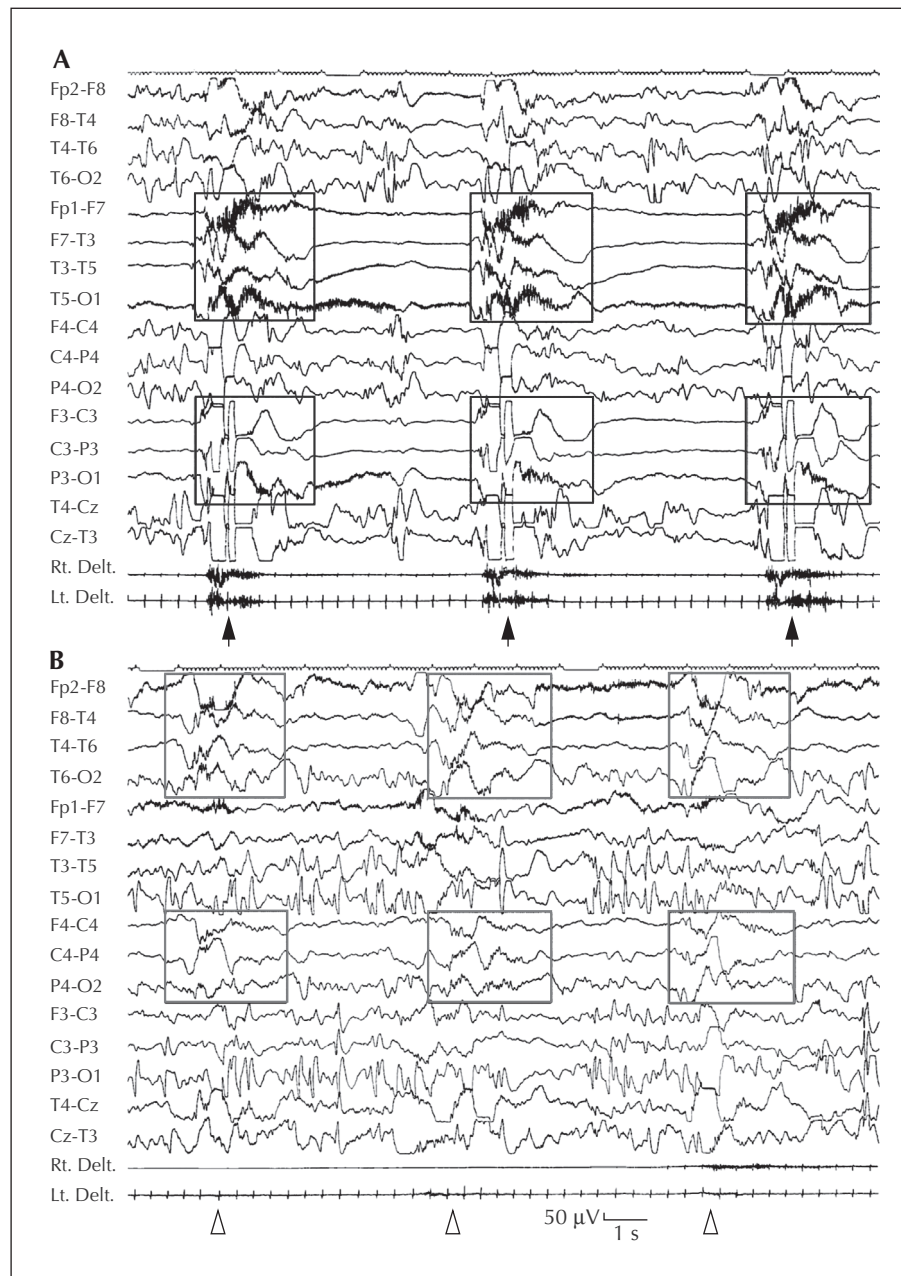


Figure 2. Ictal EEGs of two different types of epileptic spasm. Type A spasms were associated with left-hemispheric HVS (**A**: closed arrow, rectangle), and type B spasms with right-hemispheric HVS (**B**: open arrowhead, rectangle). In each type of spasm, the contralateral hemisphere showed interictal hypsarrhythmia with periodicity.

similar to those observed in the current patient, indicate a link between the behaviourally more involved side and the contralateral EEG discharges (Gaily *et al.*, 1995). The present patient had malformation involving the bilateral frontal lobes, and therefore it is possible

that her cortical dysplastic lesion played a role in the generation of ES with such complex asymmetric manifestations. Her brain malformation may not be exactly symmetric because the two types of ES had considerably different semiology. However, this is not to say that

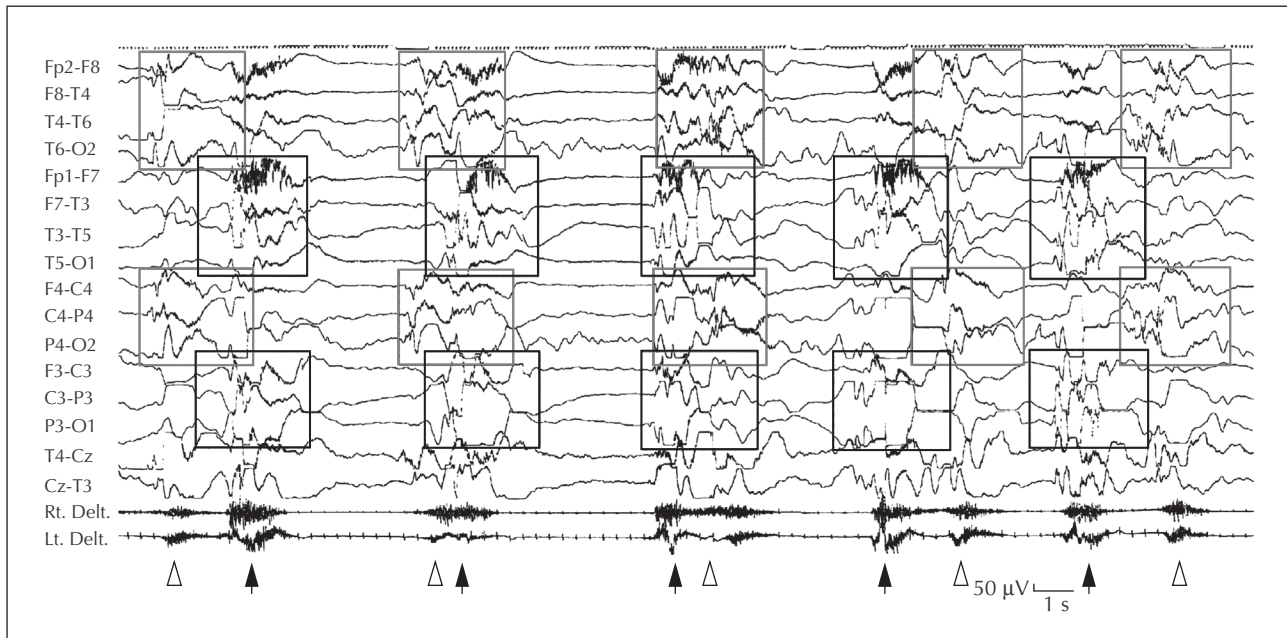


Figure 3. Concurrence of two different types of epileptic spasm. Left-hemispheric HVS associated with type A spasms (closed arrow, black rectangle) and right-hemispheric HVS associated with type B spasms (open arrowhead, grey rectangle) appear independently, each type maintaining an independent intrinsic interval.

the subcortical structures play no role at all, as there are reports of activation of the brainstem in West syndrome (Chugani *et al.*, 1992; Siniatchkin *et al.*, 2007). In this context, it is worth noting that the concurrence of two different types of spasm with no mutual interaction was successfully recorded. This fact demonstrates that the brainstem can be stimulated by each hemisphere independently. This observation failed to support the hypothesis that the brainstem always plays an initiating role in generating spasms. Although it may be impossible to generalise this notion of absolute secondary involvement of the brainstem to all infants with ES, the current case provides an important clue concerning the pathogenesis of ES confined within the cortex. □

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Legends for video sequences

Video sequence 1

Type A spasms in series with simultaneous EEG recording (indicated as “A” in red).

Video sequence 2

Type B spasms in series with simultaneous EEG recording (indicated as “B” in blue).

Video sequence 3

Concurrence of type A spasms (indicated as “A” in red) and type B spasms (indicated as “B” in blue) with simultaneous EEG recording. When the two types of spasm concurred, each type maintained independent pace and ictal symptomatology with no apparent mutual interaction.

Key words for video research on www.epilepticdisorders.com

Etiology: Aicardi syndrome

Phenomenology: spasm (epileptic)

Localization: hemispheric, multifocal

Syndrome: epileptic encephalopathy not otherwise classified

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