

# Startle-induced seizures associated with infantile hemiplegia: implication of the supplementary motor area

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**ABSTRACT** – This case illustrates an uncommon form of symptomatic startle-induced epilepsy associated with infantile hemiplegia. Seizure semiology, neuroimaging and neurophysiological findings support involvement of the supplementary motor area in the generation of this seizure type. We present the case of an 11-year-old girl with an uncommon form of startle-induced seizures, illustrated on video-EEG, against the background of left infantile hemiplegia associated with extensive right hemispheric porencephaly but preserved cognitive functioning. The epileptic focus appears to be in the dorsolateral frontal lobe, with seizure semiology involving the supplementary motor cortex. [Published with videosequences]

**Key words:** reflex seizures, startle epilepsy, supplementary motor area, MEG, epilepsy surgery

## Case report

This child presented, at 11 years of age, with an initial seizure consisting of an inability to move her left leg, and then her left arm, lasting approximately one minute, before secondarily generalizing. She was started on carbamazepine, with which this initial seizure type remains well controlled. Within a week of the first seizure described above, she also developed “freezing” episodes that continue to occur daily. These are precipitated by a sudden, surprising stimulus that may be auditory, visual or tactile. For example, a sudden loud noise such as a balloon popping, or running into someone accidentally in a crowd, will precipitate the event. After each at-

tack, she describes that she was unable to move or respond for several seconds, but was fully aware.

The semiology of this seizure type is characterized by abrupt tonic posturing of the left arm and hand, also usually involving the left leg. She occasionally falls if standing. While postured, the left arm and leg exhibit myoclonic movements. There is posturing of the left hand with extension of the fingers. In most events, the right arm is flexed in a tonic posture, but the right leg is not involved. Vocalization and a look of fear and distress accompany the abnormal posture. Her neck is flexed, with myoclonic movements of the head towards the left, but there is no hemifacial involvement. There is no eye version. After 10-20 seconds,



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the ictus ceases spontaneously and she is distressed but responsive to those around her with no significant post-ictal state. She has full recollection of each attack, although she cannot speak during the episode, and she does not experience any aura or sensory symptoms associated with these events. A typical event is illustrated on the accompanying video (*see video sequence*). Carbamazepine alone, and in combination with gabapentin or clobazam, has failed to control these seizures.

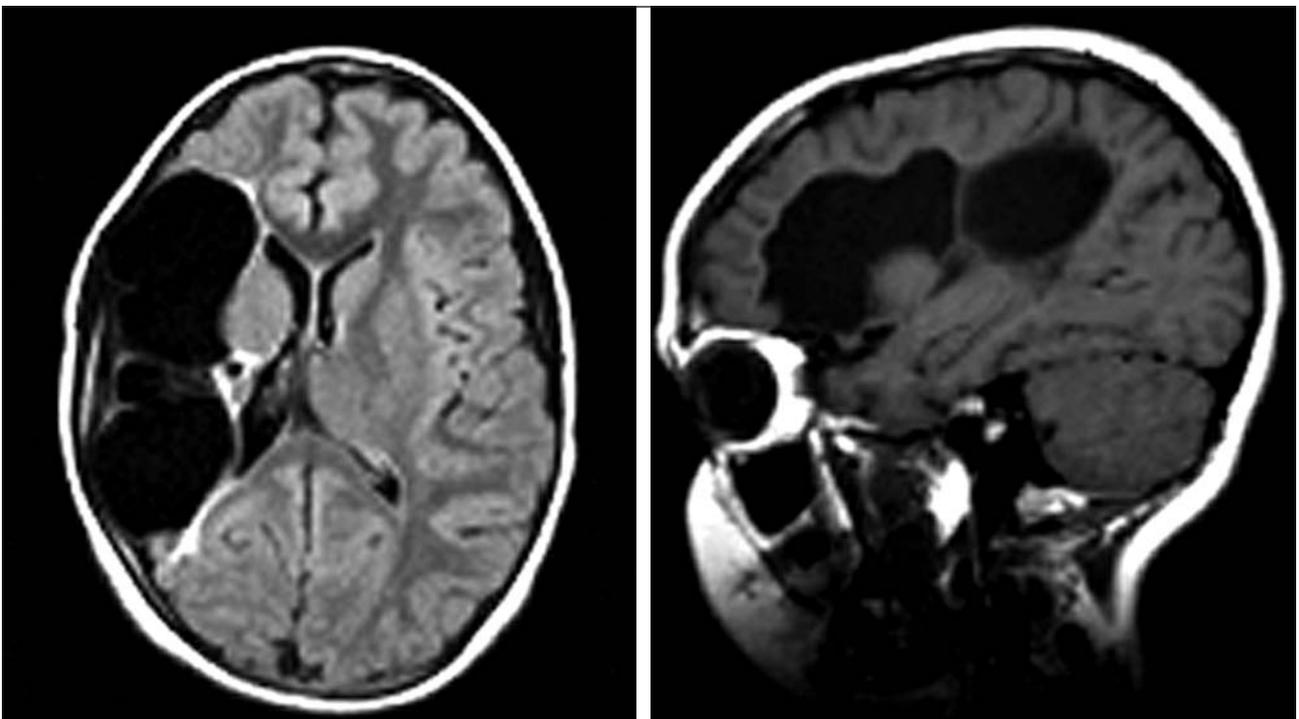
The child was born at term after a pregnancy complicated by severe maternal hypertension, but did not have any clinical neonatal problems. From six months of age she was noted to demonstrate a right-handed preference, associated with left-sided weakness. A head CT scan at nine months identified a large, right-hemispheric, porencephalic cyst, presumed to be due to an intrauterine, ischemic event. Despite her moderate, left-sided hemiplegia, her development progressed well. She was walking by 16 months, and had no difficulties with speech or intellectual development. She has had considerable difficulties with fine motor movements of the left hand. She is currently in grade 8, maintaining passing grades and participating in most activities in the normal curriculum.

On examination, she is a sociable and cooperative girl with normal, overall growth percentiles. Growth asymmetry is apparent, with a shorter left leg and smaller left hand compared to the right side. She has moderate hemiplegia, with prominent, left upper limb weakness and marked

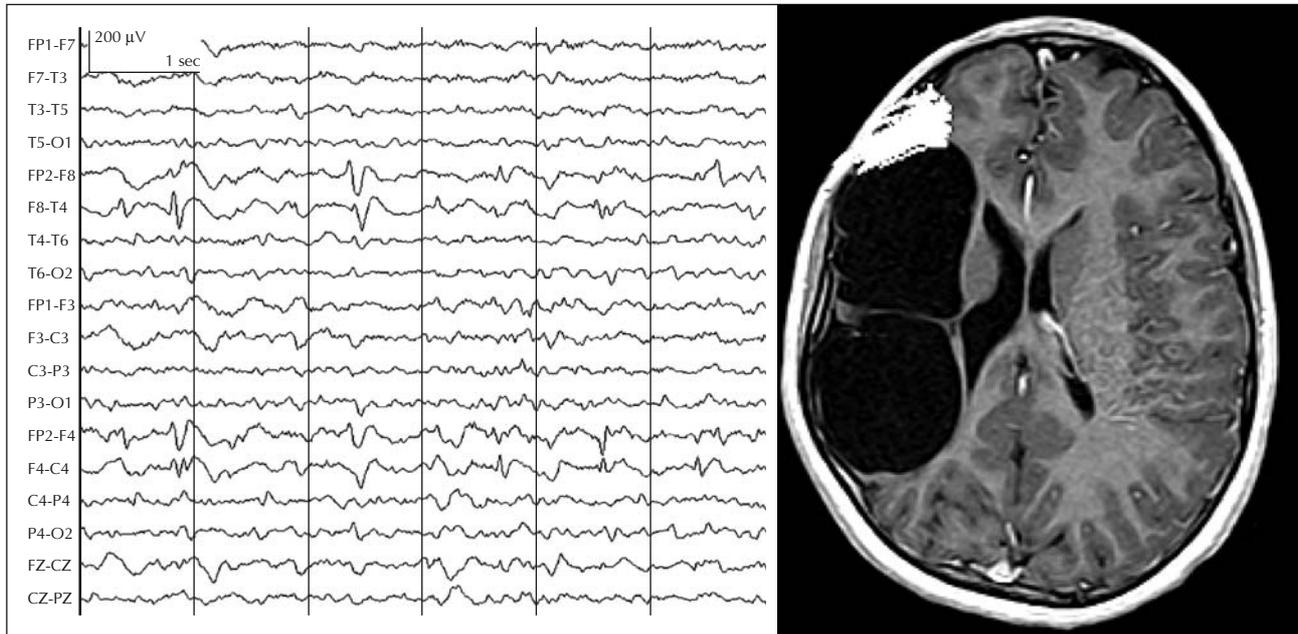
weakness of fine motor movements of the left hand. She also has some sensory deficits, with difficulty in proprioception of the left arm and leg, but intact pain and temperature sensation. She has no visual field deficit.

Neuroimaging by MRI confirmed a very large region of cystic encephalomalacia in the region supplied by the right middle cerebral artery. This cystic area extended through the frontal, temporal and parietal regions, with preservation of the caudate head but not of the caudate body or posterior lentiform nucleus. In addition, there is evidence of cortical malformation with thickening of the remaining cortex in the right frontal lobe (*figure 1*). The left hemisphere was normal.

During the first VEEG monitoring, at 11 years of age, five clinical seizures were recorded, all precipitated by a startle: no unprovoked seizures occurred. The semiology of each event was stereotyped. The ictal correlate of these events was of fast activity in the alpha frequency range, 10-12Hz, from the right central region, evolving into rhythmic spike and wave in the right fronto-central and slowing in the right temporal regions. The interictal EEG demonstrated frequent, right fronto-central spike and wave, with maximum negativity at FP2, F8 and F4, and marked activation in sleep (*figure 2*). No independent discharges were seen over the left hemisphere. Magnetoencephalography (MEG) confirmed the right frontal, epileptic focus, with a tight cluster of epileptic dipoles seen in the right frontal cortical malformation (*figure 2*).



**Figure 1.** Axial FLAIR and sagittal T1 MR images demonstrating a large region of porencephaly in the distribution of the right middle cerebral artery, with preservation of the caudate head. Evidence of cortical malformation is seen, with abnormal thickening of the right frontal cortex.



**Figure 2.** Interictal EEG demonstrating frequent, right fronto-central spike and wave, with maximum negativity at FP2 (left). Magnetic source image showing a tight cluster of interictal MEG spike sources (white arrows) at the anterior margin of the porencephalic cyst in the right frontal region (right).

The second VEEG, at 12 years of age, captured nine seizures, with a mixture of startle-provoked and spontaneous seizures after withdrawing antiepileptic medications. The semiology of each event was identical and similar to those of the first VEEG. Ictal EEG showed low amplitude, beta fast waves in the right fronto-central regions at the start of the left upper limb posturing and right arm flexion, followed by repetitive, slow waves accompanied by clonic movements (see *video sequence*).

## Discussion

This case illustrates an uncommon form of symptomatic, startle-induced epilepsy, with the epileptic foci most likely originating in or adjacent to the supplementary motor area (SMA). This child had a presumed intrauterine brain injury affecting the entire right hemisphere, resulting in large areas of cystic encephalomalacia and malformation of the remaining cortex. She presented with focal onset, secondarily generalized seizures at 11 years of age, which were easily controlled. Concurrently, she had medically intractable, reflex tonic seizures, precipitated in a very stereotyped manner by any startling event, whether auditory, visual or tactile, although most stimuli were auditory. The tonic seizures experienced by this child have the characteristic features arising from the SMA (Morris *et al.* 1988, Chauvel *et al.* 1992). They consist of the abrupt onset of asymmetric tonic posturing of the extremities, with vocalization and speech arrest, preserved conscious-

ness and brief duration, with no post-ictal state. An associated sensation of fear or anguish is reported, as well as post-ictal alteration in mood (Chauvel *et al.* 1992). Seizures with this classic semiology are likely to originate from an ictal onset zone within or adjacent to the SMA, or with rapid propagation to the SMA. Previous reports have also attributed startle epilepsy, in the context of perinatal or infantile brain damage and contralateral hemiplegia, to a focus arising in the frontal lobe (Aguglia *et al.* 1984, Saenz-Lope *et al.* 1984, Chauvel *et al.* 1992, Manford *et al.* 1996, Oguni *et al.* 1998). Surgical resection of large regions of the frontal lobe including the SMA and adjacent sensorimotor areas in similar cases, have resulted in seizure-freedom post-operatively (Oguni *et al.* 1998, Serles *et al.* 1999). These examples further implicate a region of abnormally excitable tissue in the dorsolateral frontal lobe and the SMA being involved in the generation of startle-induced seizures. The network involved is not clear, and multiple mechanisms have been proposed (Chauvel *et al.* 1992, Oguni *et al.* 1998), most suggesting a low threshold for excitability involving the motor and/or premotor areas.

Although an uncommon seizure type, small series have been reported of up to 20 patients. In these series, the most common etiology appears to be perinatal anoxia or hypoxia (Aguglia *et al.* 1984, Saenz-Lope *et al.* 1984, Chauvel *et al.* 1992, Manford *et al.* 1996). Large, unilateral, atrophic regions are usually documented on neuroimaging, involving cortex and subcortical structures (Chauvel *et al.* 1992). The association of cortical dysplasia with this

seizure type has become more evident with the advent of more sophisticated neuroimaging (Aguglia *et al.* 1984, Saenz-Lope *et al.* 1984, Manford *et al.* 1996). In this presented case, neuroimaging demonstrates coexisting cortical dysplasia. This interesting combination has been documented previously, with reports of histologically confirmed polymicrogyria and coextensive cortical necrosis (Caviness *et al.* 1978).

The majority of cases of startle-induced epilepsy occur in children with infantile or earlier onset brain injury, and most affected children have moderate to severe intellectual disturbance (Aguglia *et al.* 1984, Saenz-Lope *et al.* 1984). However, a minority of cases have relative preservation of cognitive function, and may even have no apparent neurological deficit (Aguglia *et al.* 1984, Saenz-Lope *et al.* 1984, Manford *et al.* 1996). In a reported series of 14 children, two distinct groups were apparent (Saenz-Lope *et al.* 1984). The group with unilateral hemispheric lesions, predominantly associated with contralateral hemiparesis, presented with higher cognitive function, seizures limited to the hemiparetic side and EEG most active in the areas identified as abnormal on neuroimaging. Our case resembles this group. The other group consisted of children with severe intellectual deficits, bilateral motor deficits, generalized seizure semiology and ictal EEG and neuroimaging showing extensive bilateral lesions.

Typically, startle-induced epileptic seizures consist of brief tonic seizures, occurring with high frequency, and usually refractory to medical therapy (Aguglia *et al.* 1984, Saenz-Lope *et al.* 1984, Manford *et al.* 1996), although benzodiazepines have shown some efficacy in small, retrospective series (Aguglia *et al.* 1984, Manford *et al.* 1996). Surgical resection has been successful. Three cases involving invasive monitoring with subdural grids to map the ictal onset zone and guided focal resection, have been reported (Oguni *et al.* 1998, Serles *et al.* 1999). In all three, the supplementary motor area was involved in the ictal onset zone and was included in the resected area. Good response to surgery was reported, with resolution of the startle-induced seizures, with approximately two years of follow-up. Further evidence suggests that intraoperative electrocorticography and localized guided excision may be effective in patients with intractable epilepsy secondary to porencephaly (Iida *et al.* 2004), also allowing preservation of motor and visual function that may have been lost with hemispherectomy. Considering the disabling social effects of this seizure type, as well as the risk of injury from unprotected falls, surgical management may result in con-



#### Legend for video sequence

This segment begins with the child sitting in bed. Her mother made a loud noise, triggering a reflex seizure with asymmetric tonic posturing and extension of the left upper limb, including the fingers, head tilting to the left side and flexion of right arm, and clonic movements, lasting 10 seconds. Post-ictally, she is distressed but aware of her surroundings.

siderable benefit to this patient, and is currently being pursued. □

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