Rare disease

Adult onset startle epilepsy

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Correspondence to Dr Brian Darryl Moseley, moseley.brian@mayo.edu**Summary**

A 45-year-old gentleman presented for classification of spells precipitated by startle. During these spells, he would briefly lose awareness, develop tonic stiffening of his extremities and fall. He had previously been diagnosed with paroxysmal kinesogenic dyskinesia and treated unsuccessfully with clonazepam, levetiracetam and carbamazepine. The patient was admitted for prolonged video EEG monitoring, during which numerous spells induced by startle were captured. His EEG revealed brief, fast beta activity in the midline central head region during each spell consistent with startle epilepsy. The present case demonstrates that startle epilepsy can rarely be diagnosed in adults; typically seizure onset in this condition is during infancy to childhood. Our patient's ictal EEG further implicates mesial structures in the generation of startle-provoked seizures. Although our patient continued to have startle-provoked seizures at last follow-up, his improvement on lamotrigine supports observations that this anticonvulsant can reduce seizure frequency and resulting morbidity.

BACKGROUND

Startle epilepsy is a rare form of reflex epilepsy, or condition in which seizures are reliably induced by sensory stimuli. Startle-provoked seizures typically arise between the ages of 10 months and 14 years and are seldom diagnosed in adults.^{1–3} The presumed insults resulting in startle epilepsy (including hypoxic-ischaemic injury, central nervous system infection and traumatic brain injury) often occur in the perinatal or postnatal period.^{1–4} Although the exact cerebral structures responsible for the generation of startle-provoked seizures have not been fully elucidated, mesial structures, including the supplementary motor area (SMA), precuneus and primary motor/somatosensory areas, have

been suggested by some.¹ Startle epilepsy is important to diagnose, as the prognosis of this condition differs from other startle syndromes. The majority of patients are refractory to anticonvulsants. In addition, many patients who develop this condition early in life will develop cognitive dysfunction as a result of continuing seizures.²

CASE PRESENTATION

A 45-year-old gentleman presented for spell classification. For the past 8 years, the patient had experienced brief spells precipitated by startle. He would develop an epigastric rising sensation, lose awareness for 1–2 s, develop tonic stiffening of his extremities and fall. He had previously

Figure 1 EEG demonstrating brief, fast beta activity in the midline central head region during startle-induced spells, consistent with seizures.

been diagnosed with paroxysmal kinesogenic dyskinesia. Despite treatment with clonazepam, levetiracetam and carbamazepine, the patient continued to have spells once to twice per week. His neurologic examination (including mental status, cranial nerve, strength, sensation, reflex, cerebellar and gait testing) was within normal limits.

INVESTIGATIONS

Laboratory testing revealed a normal complete blood count, thyroid stimulating hormone of 1.2 mIU/l (reference range 0.3–5.0), ceruloplasmin enzyme level of 21.5 mg/dl (reference range 14.0–21.9), and normal paraneoplastic panel. An MRI brain revealed no abnormalities. The patient was subsequently admitted for prolonged video EEG monitoring. Numerous spells induced by startle were captured (video 1). During these events, the patient briefly lost awareness. This was demonstrated by his inability to remember a memory phrase given to him during one of the spells. He then developed tonic stiffening and would have fallen if not supported by a harness. Each spell lasted for less than 5 s, followed by regaining of consciousness and no residual confusion. His EEG revealed brief, fast beta activity in the midline central head region during each spell (figure 1).

Video 1 Startle induced spells captured on prolonged video EEG.10.1136/bcr.09.2011.4801v1

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for startle syndromes is broad. It includes hyperekplexia, paroxysmal kinesogenic dyskinesia, startle epilepsy, reticular and propriospinal myoclonus, cataplexy, stiff person syndrome, exaggerated startle response (including from Creutzfeldt–Jakob disease or subacute sclerosing panencephalitis), and neuropsychiatric conditions (such as hysterical jumps, anxiety disorders and Tourette's syndrome).⁵ The patient's history was not suggestive of hyperekplexia, as the onset of his symptoms occurred during adulthood. Patients with the major form of hyperekplexia (often caused by an autosomal dominant mutation in the $\alpha 1$ subunit of the glycine receptor gene *GLRA1*) typically develop generalised stiffness shortly after birth.⁵ Although this often resolves during the first few years of life, excess startle responses followed by generalised stiffness lasting a few seconds persist. His presentation was also atypical for the minor form of hyperekplexia (startle response without generalised stiffness); symptoms in this disorder typically develop between infancy and puberty.⁵ Although the patient had been diagnosed with paroxysmal kinesogenic dyskinesia elsewhere, this diagnosis was questioned given his brief loss of consciousness with each spell. In addition, his lack of response to anticonvulsants would be atypical for this condition.⁶ Given the results of his investigation (including prolonged video EEG revealing midline epileptiform discharges with each spell), the patient was diagnosed with startle epilepsy.

TREATMENT, OUTCOME AND FOLLOW-UP

The patient was discharged on phenytoin. Despite titrating up to a dose of 200 mg twice daily, the phenytoin resulted

in no reduction in seizure frequency. He was subsequently transitioned to lamotrigine, titrating up to a dose of 100 mg in the morning, 200 mg in the afternoon, and 100 mg in the evening. Although the switch to lamotrigine improved his seizure control, he continued to have startle-provoked seizures every 1–2 weeks almost a year later.

DISCUSSION

Startle epilepsy is a rare form of epilepsy. In contrast to our patient, startle-provoked seizures typically arise during infancy to childhood.^{1–3} Although patients with normal neuroimaging have been described,⁷ most have abnormalities. These include porencephalic lesions, cortical dysplasia, periventricular lesions, subdural hematomas, delayed myelination and varying degrees of cerebral atrophy.^{1–3} Tonic seizures are most commonly observed in this condition. However, myoclonic, absence, tonic-clonic and partial seizures have been reported.^{2,3} The corresponding EEG often reveals a diffuse electrodecremental pattern³; however, focal epileptiform activity has been reported.^{1,7} The location of our patient's ictal discharges further implicates mesial structures in the generation of startle-provoked seizures. This is supported by ictal single photon emission CT, which has demonstrated consistent hyperperfusion over the mesial frontocentral region (including the SMA, the perirolandic region and the precuneus) during such seizures.¹

As was demonstrated in our case, startle epilepsy can be mistaken for other startle syndromes. Proper diagnosis of startle epilepsy is important, as its prognosis differs from its mimickers. Similar to our case, the majority of patients are refractory to anticonvulsants. However, certain medications (particularly lamotrigine) have been reported to help to reduce seizure frequency and intensity.^{8,9} This can result in reduced morbidity, improving overall quality of life.

Learning points

- ▶ Startle epilepsy is a rare form of reflex epilepsy that should be considered in the differential of someone presenting with a startle syndrome.
- ▶ Although startle epilepsy is typically diagnosed during infancy to childhood, it can rarely be diagnosed in adults.
- ▶ The gold standard for diagnosing startle epilepsy is video-EEG. Although the corresponding EEG often reveals a diffuse electrodecremental pattern, focal epileptiform activity can be seen.
- ▶ Startle-provoked seizures may be generated by mesial structures, including the SMA, precuneus and primary motor/somatosensory areas.
- ▶ The majority of patients with startle epilepsy are refractory to anticonvulsants. However, certain medications (particularly lamotrigine) may help to reduce seizures.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Fernández S**, Donaire A, Maestro I, *et al*. Functional neuroimaging in startle epilepsy: Involvement of a mesial frontoparietal network. *Epilepsia* 2011;**52**:1725–32.
2. **Yang Z**, Liu X, Qin J, *et al*. Clinical and electrophysiological characteristics of startle epilepsy in childhood. *Clin Neurophysiol* 2010;**121**:658–64.
3. **Tibussek D**, Wohlrab G, Boltshauser E, *et al*. Proven startle-provoked epileptic seizures in childhood: semiologic and electrophysiologic variability. *Epilepsia* 2006;**47**:1050–8.
4. **Guerrini R**, Genton P, Bureau M, *et al*. Reflex seizures are frequent in patients with Down syndrome and epilepsy. *Epilepsia* 1990;**31**:406–17.
5. **Bakker MJ**, van Dijk JG, van den Maagdenberg AM, *et al*. Startle syndromes. *Lancet Neurol* 2006;**5**:513–24.
6. **Houser MK**, Soland VL, Bhatia KP, *et al*. Paroxysmal kinesigenic choreoathetosis: a report of 26 patients. *J Neurol* 1999;**246**:120–6.
7. **García-Morales I**, Maestú F, Pérez-Jiménez MA, *et al*. A clinical and magnetoencephalography study of MRI-negative startle epilepsy. *Epilepsy Behav* 2009;**16**:166–71.
8. **Ikeda H**, Imai K, Ikeda H, *et al*. Lamotrigine is favourable for startle-induced seizures. *Epileptic Disord*. Published Online First: 6 Sep 2011. doi: 10.1684/epd.2011.0458
9. **Faught E**. Lamotrigine for startle-induced seizures. *Seizure* 1999;**8**:361–3.

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