Epileptic Disord 2012; 14 (2): 167-71

Late-onset, praxis-induced myoclonic epilepsy

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Received January 27, 2011; Accepted February 29, 2012

ABSTRACT – Praxis-induction of seizures is an interesting subset of reflex epilepsy in which seizures are induced by higher mental activities associated with the use of part of the body. Reflex traits have often been described in patients with juvenile myoclonic epilepsy. We report a patient presenting with praxis-induced myoclonic epilepsy at a late age. Ictal myoclonus was triggered by building a bird house and captured by video-polygraphic EEG recording. At 39 years old, the patient's age at onset of epilepsy was consistent with the syndrome of adult myoclonic epilepsy. Our case supports the notion of adult myoclonic epilepsy with possible occurrence of praxis-activation of seizures, as has been noted with the other idiopathic generalised epilepsies. [*Published with videosequences*]

Key words: myoclonic epilepsy, praxis-induced seizures, reflex seizures

The term "praxis-induced epilepsy" was introduced by Inoue *et al* (1994) for patients whose seizures are provoked by contemplating complicated spatial tasks in a sequential fashion, making a decision and responding by using part of the body (Inoue *et al*., 1994; Ferlazzo *et al*., 2005). Seizure susceptibility to higher mental activities appears to be higher for the idiopathic generalised epilepsy (IGE) syndromes, particularly for juvenile myoclonic epilepsy (Matsuoka *et al*., 2000; Mayer *et al*., 2006).

Herein, we present a case of late-onset praxis-induced myoclonic epilepsy occurring after head trauma.

Case Report

A 46-year-old Hispanic right-handed man with medical history significant for insomnia, traumatic brain injury, major depressive disorder, and low back pain, was admitted to our hospital for evaluation of a two-year history of intermittent body jerks. These episodes only occurred while performing manual tasks, including typing, sanding wood, or hanging party decorations. Tasks which induced the jerks were impossible for him to complete in one sitting as continuation of the task induced a crescendo interference. In frustration, he would abandon the task,

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doi:10.1684/epd.2012.0498

perhaps being able to complete it hours later. He denied impaired awareness during these episodes. Sleep deprivation and tiredness augmented the propensity for the task-interfering jerks.

He reported a forceful fall seven years ago while performing a military step march with his platoon, carrying a 70-pound backpack. He did not lose consciousness, but was momentarily dazed as the back of his head hit the backpack. About two weeks later, he recalled having a violent episode of jerking while packing a suitcase. He grabbed a shirt and instantly had an upper body jerk that was so forceful it caused him to throw the shirt across the room. He denied ever having similar jerks in the past prior to the fall, even with sleep deprivation or alcohol use. He had no other risk factors of epilepsy such as family history of seizure, febrile seizures, prematurity, or previous central nervous system infections. His psychiatric condition was being managed successfully with aripiprazole and venlafaxine, and his chronic lower back pain was under reasonable control with a combination of baclofen, gabapentin, hydrocodone/acetaminophen, and morphine sulfate. There had been no major changes to the medication regimen for the past three years. A neurological examination and routine blood tests were normal. Compared to before admission, brain MRI was unchanged and unremarkable.

Continuous EEG-video monitoring was carried out under sleep deprivation. The patient was given several craft kits to work on. Frequent myoclonic jerks were captured while he attempted to build a bird house using building blocks. Continuing the task increased the occurrence of the myoclonic jerks and his level of frustration. Myoclonic jerks observed predominantly involved the upper extremities and shoulder, with occasional accompanying neck flexing and/or eye blinking. While not rhythmic, there was a tendency for clustering during portions of the task that required manipulation of the building blocks. They did not occur when he simply imagined performing the task or during sleep. EEG correlation demonstrated high-amplitude (100 microvolt) generalised spike-and-slow wave complexes, about 2/second, which were very brief (100 milliseconds) and had a frontocentral predominance (*figure 1*). During a period of 48 hours of monitoring, only three isolated myoclonic jerks with EEG spike-wave correlate were captured which were not associated with any particular activity. EEG demonstrated an otherwise normal background and a negative response to photic activation.

The patient was started on low-dose valproic acid twice daily. This was eventually changed to once daily for medication compliance and avoidance of side effects. One year later, he reported no further episodes.

Discussion

Reflex epilepsy is a well-recognised subset of epileptic disorders in which seizures are induced by specific

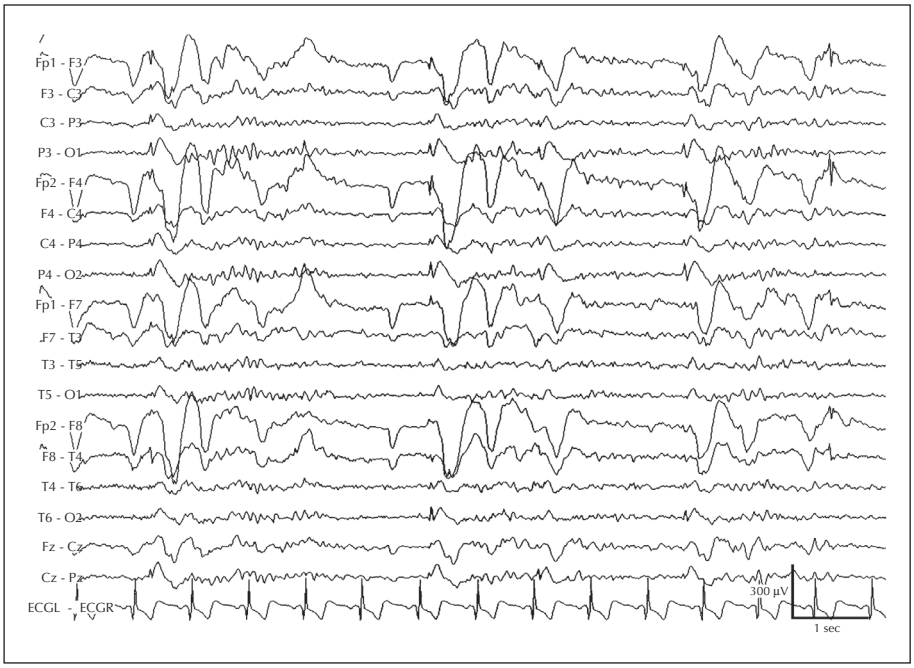

Figure 1. Standard EEG while building a bird house (*amplitude: 15 microvolts/mm; time constant: 0.1; filter: 30 Hz*) showing intermittent spike-wave discharges, maximum in frontal areas with alternating eye blinks. Spike-and-wave discharges correlate with myoclonic jerks.

extrinsic, or less commonly, intrinsic stimuli. It occurs in 5% of patients with epilepsy (Inoue *et al*., 1994). Individuals may have solely reflex seizures, or these may co-exist with other epilepsy disorders. Reflex seizures may manifest as partial or generalised seizures and can be symptomatic, cryptogenic, or idiopathic. They are often classified according to the stimuli that triggers them rather than by the type of seizure produced. The most recognised form of reflex epilepsy is photosensitive epilepsy (Ferlazzo *et al*., 2005).

Praxis-induced epilepsy is a subset of the reflex epilepsies. Inoue and colleagues reported a series of 21 patients whose seizures were induced by non-verbal, praxic activities accompanied by games, calculations, drawing, writing, or constructions. A combination of decision making along with motor activities involving the hands and fingers was considered to be the seizure-induction mechanism (Inoue *et al*., 1994). A prospective investigation of this phenomenon was carried out by Matsuoka and colleagues in 480 patients with a wide representation of seizure types using a battery of neuropsychological EEG activation tasks which included spatial constructions (Matsuoka *et al*., 2000). Higher non-verbal activities provoked EEG epileptiform discharges in 8% of patients, with myoclonic and absence seizures being the most common types elicited. Tasks that required additional use of the hands such as writing, written calculations and spatial constructions were more likely to trigger epileptiform discharges/seizures. Thirty-six of the 38 identified patients had an idiopathic generalised epileptic syndrome, with juvenile myoclonic epilepsy (JME) accounting for 22 of the patients. In their series, a total of 45 patients with JME were screened with the activation battery, which suggests that the phenomena of praxis-induced myoclonic seizures could be present in up to half the JME patients. Guaranha and colleagues applied a neuropsychological activation battery to a group of 71 JME patients. Their work confirmed the relative high occurrence of praxis-induced myoclonus in JME patients (38%) which was neither dependent on treatment nor on seizure control, suggesting it to be a true reflex trait. The complexity of the task, *i.e*. two *versus* three-dimensional constructions, correlated with the effectiveness in precipitating the reflex myoclonus (Guaranha *et al*., 2009). The semiology of the praxis-induced myoclonic jerk predominantly involves the upper extremities and shoulder, however, perioral and periocular myoclonia may go unobserved (Mayer *et al*., 2006).

Praxis, or the production of learned skilled movements, is mediated by a modular network of cortical and subcortical structures that may include the thalamus. The thalamus has been posited to function as a gated relay to filter out irrelevant information and may selectively engage relevant cortical networks. Thalamic lesions have been associated with apractic deficits (Ohno *et al*., 2000). The cortico-thalamic system is organised to play a key role in synchronising the activities of thalamic and cortical neurons (Jones, 2009). EEG-functional MRI studies in patients with various idiopathic generalised epilepsies have demonstrated a thalamic increase in blood oxygenation level-dependent signals along with regional decreases in the fronto-parietal cortex and the caudate nuclei during generalised spike-and-wave EEG discharges (Moeller *et al*., 2008). It is reasonable to postulate cross-activation of striatal-thalamic-cortical networks as the mechanism involved in praxis-induced myoclonic jerks in the idiopathic generalised epilepsies.

An alternative mechanism of seizure generation, similar to that of photosensitive epilepsy, is the requirement of excitation of a hyperexcitable area associated with proprioceptive input, which then propagates to the adjacent motor cortex through a direct transcortical pathway generating myoclonus (Hallet, 1985). Ferlazzo and colleagues proposed that a stimulus must be strong enough to activate a critical mass of cortex to produce epileptic activity (Ferlazzo *et al*., 2005). For example, cognitive tasks requiring the use of hands were found to be more epileptogenic than complex mental activities not requiring the use of hands. Similarly, hand movements without associated cognitive stimuli, *i.e*. finger tapping or drawing meaningless lines, were not effective in triggering seizures in patients with praxis-induced epilepsy (Matsuoka *et al*., 2000).

Our patient's first myoclonic seizure occurred while participating in a military step march at the age of 39 years. A myoclonic seizure could have resulted in the loss of balance, compounded by the excessive 70-pound backpack and subsequent mild head injury. A military step march is a regular, ordered and synchronised walk with military formation. The sequential and spatial positioning of the body requires a constant and fairly high level of concentration for a flawless execution, *i.e*. praxis. The physical stress of the drill could have contributed to both the myoclonic seizure and/or the fall.

While the age at onset of JME occurs by the second decade of life, late-onset cases have been described. Whether this subset of late-onset cases represents a distinct syndrome within the IGEs remains to be settled (Cutting *et al*., 2001; Reichsoellner *et al*., 2010). In a comprehensive review of 492 IGE patients, Reichsoellner and colleagues found the expected age-at-onset distribution to be up to the age of 30. From the fourth decade on, the distribution was skewed by a handful of cases older than 40; only 6% of patients had a seizure onset after the age of 30 years. Generalised tonic-clonic (GTC) seizures were the predominant seizure type at presentation (86% of cases), while

myoclonic seizures were the initial seizure in only two (7%) of their late-onset cases (Reichsoellner *et al*., 2010). Another large series of 313 cases demonstrated a higher number of patients experiencing myoclonic seizures; 50% of late-onset IGE cases (Cutting *et al*., 2001). Apart from the age at onset, none of these patients differed from their younger counterparts in terms of normal neurological examination, EEG features, excellent response to antiepileptic medical treatment, and good prognosis (Cutting *et al*., 2001; Reichsoellner *et al*., 2010).

We believe the diagnosis of our patient fits the IGE subgroup of adult myoclonic epilepsy (AME). Two case series identified AME in 6 and 11 patients with mean ages at onset of 37 and 39 years, respectively (Gilliam *et al*., 2000; Marini *et al*., 2003). The late presentation of praxis-induced seizures in the AME series reviewed was not specifically discussed (Gilliam *et al*., 2000; Cutting *et al*., 2001; Marini *et al*., 2003; Reichsoellner *et al*., 2010) and both neuropsychological activation series encompassed relatively young patients (Cutting *et al*., 2001; Reichsoellner *et al*., 2010). While our patient only experienced myoclonic seizures, it is known that the second generalised seizure type (GTC or absences) may be infrequent and/or presents years later. Marini and colleagues reported that of their six patients with AME, the number of GTC seizures in each case was small; three patients reported only one lifetime GTC seizure, two patients reported two lifetime GTC seizures, and one patient reported three lifetime GTC seizures (Marini *et al*., 2003). Similar to our patient, Gilliam *et al*. reported that myoclonic jerks were usually isolated, but that they could occur in "flurries of repetitive jerks". In the reviewed series, as in this case, ictal EEGs showed generalised spike or polyspike-and-wave activity (Gilliam *et al*., 2000; Cutting *et al*., 2001; Marini *et al*., 2003).

The familial form of AME is associated with action finger tremors, rhythmic cortical postural myoclonus, progressively worsening myoclonus, and a clear autosomal dominant mode of inheritance (Striano *et al*., 2005). However, our patient did not report these clinical or historical features. Other authors have identified patients with idiopathic adult-onset myoclonic seizures who lack this clinical phenotype and autosomal familial inheritance (Gilliam *et al*., 2000; Marini *et al*., 2003). These authors suggest that the adult-onset IGE subgroup of AME is a clinical syndrome distinct from familial AME.

Our case report has several limitations. Medications may have influenced the precipitation of seizures. The onset of myoclonus predated the prescription of venlafaxine and aripiprazole, but his symptoms became more problematic after their introduction, raising the possibility that these medications exacerbated the seizure frequency. Our patient refused genetic testing for JME which would have helped to exclude this diagnosis. In addition, he did not return to our clinic for testing of giant somatosensory evoked potentials typical for AME (Striano *et al*., 2005), evidence which would have strengthened our report.

Despite these limitations, our case supports the notion of adult myoclonic epilepsy with possible occurrence of praxis-activation of seizures, as in other IGEs; the degree of occurrence remains to be determined. □

Acknowledgements.
We would like to thank Maria Resillez, REEGT, for video-EEG technical assistance.

Disclosures.
None of the authors has any conflict of interest to disclose.

Legend for video sequence

Ictal myoclonus while building a bird house. Myoclonus interferes with task completion, resulting in frustration.

Key words for video research on www.epilepticdisorders.com

Syndrome: reflex epilepsy
Etiology: unknown
Phenomenology: reflex seizures; myoclonic seizure
Localization: not applicable

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