Case Report

Response to Levetiracetam in a Patient with Posthypoxic Action Myoclonus

Emine GENÇ, Serhat TOKGÖZ, Ebru APAYDIN DOĞAN, Bülent Oğuz GENÇ
Selcuk University Meram Faculty of Medicine, Department of Neurology, Konya, Türkiye

Abstract

Posthypoxic action myoclonus (PAM) can be developed in patients who survived an hypoxic brain injury and is resistant to pharmacological therapy. The patient presented here developed PAM with very serious myoclonic jerks by which he was fully incapacitated. His myoclonus did not respond to treatment with most commonly used agents, i.e. valproate, topiramate, clonazepam and baclofen alone or in combination. An important degree of improvement was observed after levetiracetam was started.

Keywords: Posthypoxic action myoclonus, levetiracetam

INTRODUCTION

PAM syndrome was first described by Lance and Adams in 1963. The syndrome is also known as Lance-Adams syndrome and its clinical features include mild intellectual impairment, action myoclonus, a mild to moderate degree of ataxia and resistance to conventional pharmacological agents. Lance-Adams syndrome is resulted from cerebral hypoxia and is relatively more frequently observed in recent years as a result of improved resuscitation techniques. Treatment is still based mainly on a “trial and error” method. Standard anticonvulsants such as phenytoin and phenobarbital have not produced desirable symptom control. This paper presents a man who survived an hypoxic brain injury after which he developed very serious action triggered jerks unresponsive to standard anticonvulsants and partly benefited from add-on therapy with levetiracetam. The effectiveness of levetiracetam in reducing myoclonus has been reported to be promising in posthypoxic myoclonus, progressive myoclonus epilepsy and spinal myoclonus.

CASE PRESENTATION

A 30-year-old man experienced serious burns covering more than 40% of his body including face, neck, hands and feet. He required mechanical ventilator support on admission to the intensive care unit of another medical center. Because of an accidental disconnection between the mechanical respirator and the intubation tube, he experienced anoxia for approximately 5 minutes and was
successfully resuscitated. After regaining consciousness, he developed high amplitude myoclonic jerks affecting the trunk and extremities. During his one year follow up, he has been treated with valproic acid 3500 mg/day, topiramate 400 mg/day, clonazepam 2mg/day and baclofen 15mg/day in gradually escalated doses but with no improvement. Then he was referred to our clinic for treatment of these incapacitating involuntary movements. On examination, serious scarring was observed on his face, neck, extremities and part of the body. Movements of the upper limbs including holding a glass or spoon to feed himself were precluded by serious myoclonic jerks. Sitting upright was very difficult because of truncal and extremity jerks, standing unassisted was impossible. The jerks could be evoked by a minor increase in muscle tone, causing the patient to fall. Even at rest, there were occasional myoclonic jerks in the upper limbs. The jerks were not observed during sleep but could be evoked by sudden noise. His mental status was normal. Finger to nose test could not properly evaluated because of serious jerks, coordination seemed to decrease secondary to myoclonus. No motor or sensory deficit or reflex abnormality was observed. Routine serological tests were unremarkable except for severe thrombocytopenia (45000/mm³) that was considered to be resulted from high dose valproic acid. MRI of the head and EEG were unremarkable. The patient was diagnosed with PAM. He was started on 500mg/day levetiracetam twice daily. Valproate was discontinued soon after the patient’s admittance followed by discontinuation of topiramate one week later. Platelet count was returned to baseline several days after discontinuation of valproate indicating that the drug was responsible for thrombocytopenia. Baclofen and diazepam could not be discontinued because of the increase in myoclonic jerks with even a small dose decrement. Along with levetiracetam escalating to higher doses over 1-4 weeks, he continued to take 60mg/day baclofen and 3mg/day clonazepam. When the dose of levetiracetam reached 4000mg/day, the patient could sit without support on the bed and could walk with assistance. Activities such as stretching his arm to handle a glass could be achieved with milder myoclonic jerks of lower amplitude and frequency. Myoclonic jerks at rest were completely resolved. At the two-year follow up, the patient continued to maintain this level of control with 3000 mg/day levetiracetam , 60 mg/day baclofen and 2mg/day clonazepam.

DISCUSSION

PAM is a subcortical myoclonus that affects many muscle groups and is sensitive to external stimuli such as sounds(2). It is a relatively rare syndrome, over 122 cases were reported since the original description of Lance and Adams in 1963. However, it has been more frequently reported in the recent years due to improved resuscitation techniques. Neuroimaging tests such as computed tomography or magnetic resonance imaging of the head are usually unremarkable. Multiple lacunar infarcts and white matter changes may occasionally appear in imaging due to diffuse neuronal injury resulted from the anoxic episode. EEG may show evidence of short duration spike and polyspike discharges(13) or may be completely normal, as it is in our case(10).

Anatomopathological study in two cases of PAM revealed diffuse neuronal degeneration in the neurons of the cortex, thalamus and subthalamic nuclei supporting Lance and Adams who stated that the myoclonus might be the result of repetitive firing of thalamocortical fibers mainly from the ventrolateral nucleus which is the principle relay nucleus from the cerebellum to the sensorimotor cortex(9,11). In an experimental study in rats, it was demonstrated that global cerebral ischemia caused Purkinje cell death in the vermis. The loss of
GABAergic inhibition in the fastigial nucleus after ischemia leads to diaschisis of the motor thalamus and the reticular formation which in turn is responsible for enhanced motor excitibility and myoclonus\(^\text{17}\). It has also been reported that abnormalities within the serotonergic system may play a role\(^\text{12}\).

PAM is often poorly controlled with current treatments. Standard anticonvulsants such as phenytoin and phenobarbital have not produced desirable symptom control\(^\text{13}\). Favorable response was obtained with clonazepam and valproic acid\(^\text{14}\). Improvement with valproic acid was reported to last from 4.5 months to over 2 years\(^\text{1,14}\). Clonazepam has been found very effective in controlling PAM. Valproate increases central nervous system GABA concentration, serum and brain tryptophan levels, decreases the excitatory neurotransmitter aspartate and augments the inhibitory effect of glycine. Clonazepam is thought to produce its antmyoclonic effect through facilitating GABA receptors and inhibiting dorsal raphe neurons. However the specific action responsible for antmyoclonic effect of valproate or clonazepam is not clear\(^\text{13}\).

Improvement with high dose piracetam\(^\text{7,16}\) and levetiracetam\(^\text{4,5,8,10,13,15}\) in patients with PAM was also reported. Efficacy of piracetam, a very potent antmyoclonic agent was reported many years ago first in patients with the Lance-Adams syndrome\(^\text{5}\). However, very high doses of piracetam (20-45g/day) are required in the treatment of both PAM and cortical myoclonus\(^\text{6,7}\) which is not very practical. Levetiracetam and zonisamide are novel antiepileptics that have recently been described to be effective in the control of myoclonus disorders\(^\text{10,13}\). Levetiracetam is an analogue of piracetam but its exact mechanism of action is unknown. Its side effect profile appears to be very safe except for minor decreases in RBC count, hemoglobin, hematocrit and white blood cell count. Levetiracetam was found to be effective in higher doses (3000-3500 mg/day) for the treatment of PAM than it was used as an anticonvulsant, although Krauss et al. (2001) used very low doses (1000-1250 mg/day) of levetiracetam\(^\text{5,8,10,13}\). Zonisamide has been shown to exhibit a strong inhibitory effect on convulsions of cortical origin and is thought to block sodium and T-type calcium channels\(^\text{13}\).

Although myoclonic jerks could not be completely supressed in our patient, he clearly demonstrated an improvement over the baseline, thus improving rehabilitation interventions. Different responses of the patients with PAM to the drugs may be attributed to the degree of hypoxic injury, as well as severity and distribution of myoclonic jerks\(^\text{11}\). Interestingly, levetiracetam was not found to be as effective in myoclonus of other etiologies as it was in PAM\(^\text{10}\). Because of the relative rarity of the syndrome, case controlled studies are lacking. However, levetiracetam appears to be a promising agent in the treatment of PAM.

**Correspondence to**

Emine Genç  
E-mail: eminegencduran@gmail.com

**Received by:** 01 June 2007  
**Revised by:** 02 September 2007  
**Accepted:** 06 September 2007

**The Online Journal of Neurological Sciences (Turkish) 1984-2007**  
This e-journal is run by Ege University Faculty of Medicine,  
Dept. of Neurological Surgery, Bornova, Izmir-35100TR  
as part of the Ege Neurological Surgery World Wide Web service.  
Comments and feedback:  
E-mail: editor@jns.dergisi.org  
URL: http://www.jns.dergisi.org  
Journal of Neurological Sciences (Turkish)  
Abbr: J. Neurol. Sci.[Turk]  
ISSNe 1302-1664
REFERENCES