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Successful case of Lance-Adams syndrome treatment with early use of perampanel after targeted therapeutic hypothermia

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Abstract

Perampanel (PER), approved as an antiseizure medication in 2012, is a selective non-competitive antagonist of α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors. PER is used as an add-on medication to treat partial-onset and primary generalized tonic-clonic seizures. In addition, positive effects have been reported in some patients with epileptic myoclonic convulsions in idiopathic systemic and progressive myoclonic epilepsy. We treated a male patient with post-hypoxic nonepileptic myoclonus (Lance-Adams syndrome) by adding PER to classic antiseizure medications after 10 days of targeted therapeutic hypothermia. Myoclonus movement, which showed no improvement with other antiseizure medications (valproate, levetiracetam, and clonazepam) administered for 9 days, gradually improved after PER was started. In addition, myoclonus recurred when the drug was withheld due to patient's dry mouth or pickled extremities. By reintroducing PER, myoclonus improved without other side effects. For this reason, we believe that the early introduction of PER in Lance-Adams syndrome after cardiac arrest is worth considering.

INTRODUCTION

Perampanel (PER) is an antiseizure medication (ASM) in the class of selective non-competitive antagonists of α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors.[1,2] It was approved as an adjunct treatment for patients having partial-onset seizures with or without secondarily generalized seizures with epilepsy or primary tonic-clonic seizures. PER was licensed in Europe and the United States after three phase III trials.[3-6] In some randomized controlled trials, additional effects were observed against myoclonic jerks in some patients.[7] PER has also been reported to have a potentially beneficial effect on progressive myoclonic epilepsy.[8,9] In a few cases, it has been used to treat chronic jerk movement in drug-resistant post-hypoxic myoclonus (Lance-Adams syndrome [LAS]) after several months of cardiac arrest. To the best of our knowledge, there was no case report of early introduction of PER in LAS that occurred after targeted therapeutic hypothermia (TTM). Herein, we present a case that demonstrates the effect of add-on PER introduced within 10 days after the end of TTM. Furthermore, PER was stopped due to some side effects, and myoclonus recurred; the myoclonus improved after reintroduction of PER. For these reasons, we suggest that the rapid introduction of PER in LAS can help improve the quality of life of patients.

CASE REPORT

A 53-year-old man visited the emergency department with dizziness after ingesting puffer fish. A few minutes after admitting the emergency department, the patient developed cardiac arrest due to respiratory failure induced by tetradotoxin. The patient with cardiac arrest was immediately witnessed by the physician, then cardiopulmonary resuscitation was performed. After 10 minutes of cardiopulmonary resuscitation, the patient had return of spontaneous circulation. Since the patient had a comatose mental status after return of spontaneous circulation, we performed TTM to the patient.

After TTM, he experienced drug-resistant post-hypoxic myoclonus. During admission to the intensive care unit, we could not proceed with extubation because of his almost continuous

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stimulus-sensitive polytopic myoclonic jerks. Electroencephalography recordings were repeatedly normal and showed no epileptiform discharges during myoclonic jerks. We performed brain computed tomography (CT) at the time of admission but found no clinically relevant abnormalities. Moreover, even after the myoclonus improved, we found no abnormal findings in brain magnetic resonance imaging (MRI) and single-photon emission computed tomography (SPECT). Three days after the end of TTM, the Glasgow coma scale (GCS) was 4+T+6, and he could move according to a simple command; however, unwanted myoclonic movements continued. For this reason, we prescribed 2,000 mg of levetiracetam, 1,200 mg valproic acid, and 1.5 mg clonazepam; however, his myoclonic movements could not be controlled. After 10 days of TTM, add-on PER was started at an initial dose of 2 mg. About 4 days after the introduction of PER, myoclonic jerk movement and tachypnea improved, and oxygen demand decreased. Thus, we were able to successfully extubate.

When PER was stopped due to dry mouth and numbness of the extremities, the patient complained of intentional tremors when making delicate movements such as using chopsticks. When 2mg of PER was reintroduced, the above symptoms persisted, and after increasing the dose to 4mg, these symptoms improved. After increasing the dose to 4 mg, PER related symptom including dry mouth or limbs numbness did not appear.

This allowed us to discontinue levetiracetam and clonazepam without other side effects. It has been 8 months since the incident, and the tremors have subjectively improved with the continued 4 mg PER dose. At present, he visits outpatient departments of rehabilitation medicine on foot.

DISCUSSION

Myoclonic jerks are symptoms of various central nervous system diseases and conditions. In particular, these myoclonic jerks, referred to as LAS, appear after cardiac arrest induced by respiratory failure. Therefore, LAS may initially be considered myoclonic status epilepticus. However, LAS is not a category within various epilepsy syndromes but is expressed as nonepileptic pathogenesis due to the cerebellar phenomenon caused by post-hypoxic brain damage.[10,11] Making an early diagnosis and properly managing LAS could improve the patient's functional outcome.[11] Although the sustained myoclonic movement in LAS is not usually of epileptic origin, antiepileptic drugs are recommended for treatment.[12] The mechanism of LAS is not completely understood. Research points to an imbalance between the neurotransmitters gamma-aminobutyric acid (GABA) and glutamate, a deficiency in serotonin, and possible problems with dopamine production, among other causes. For this reason, other therapeutic approaches have been devised for this behavioral disorder, and the following agents have been proposed: levodopa and GABAergic drugs[12] and L-5-hydroxytryptophan[13]; however, most AEDs did not seem to be useful.

The brain is vulnerable to secondary damage caused by ischemia, edema, and metabolic impairment after cardiac arrest.[14] TTM has been used to prevent secondary neurologic injury and improve prognosis in neonatal hypoxic-ischemic encephalopathy and out-of-hospital cardiac arrest.[14] The effect of TTM on the occurrence and severity of LAS has not been proven. Meanwhile, considering the neuroprotective effect of TTM (in the case of our patient, neruon-specific enolase -- NSE level decreased from 42.7 to 13.1), it may have a positive effect of post-hypoxic myoclonus such as LAS.

We used the recommended ASM for our patient. Upon consulting with a neurologist, we received a response that the ASM used were of adequate doses, and it may not be effective in our patient. However, since PER has been used for juvenile myoclonic epilepsy[7], acute myoclonic status after severe hypoxia[8,9], and post-hypoxic myoclonus after cardiac arrest due to Brugada syndrome.[10] Therefore, we assumed that adding PER may be effective in our patient.

The main side effects of adding PER were numbness of the feet and around the mouth.[13] Because the patient's myoclonic jerks had shown improvement and he complained of numbness around the mouth and feet, we decided to stop the drug. However, after stopping PER, myoclonus showed worsening when the patient attempted intentional movements such as using chopsticks; therefore, we reintroduced PER. The dose of PER was increased to 4 mg, according to the patient's symptoms and obtained good results. Therefore, we suggest in LAS, early add-on PER after TTM could be considered.

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