Case Report
Lance-Adams syndrome: a case report and retrospective review

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Abstract: Chronic post-hypoxic myoclonus, also known as Lance-Adams syndrome (LAS), is a rare complication of successful cardiopulmonary resuscitation characterized by action myoclonus. LAS is seen in patients who have undergone a cardiorespiratory arrest, regained consciousness afterwards, and then developed myoclonus days or weeks after the event. Another form of post-hypoxic myoclonus is acute post-hypoxic status epilepticus, which is associated with a poor prognosis. Differentiating between these two conditions is important for prognosis and medical intervention. However, it is often difficult to distinguish between them clinically. Intensive studies have suggested two indicators that differentiate between the two types: onset time of myoclonus and regaining of consciousness. Here, we describe an unusual case of LAS in which a 49-year-old woman was buried in mud for 10 minutes due to a work accident, and subsequently suffered a cardiac respiratory arrest. After successful cardiopulmonary resuscitation, she presented with post-hypoxic myoclonus early and regained consciousness very late (after 38 days). This case presents an exception to commonly used diagnosis indicators, and suggests that acute post-hypoxic myoclonus might convert into chronic post-hypoxic myoclonus.

Keywords: Lance-Adams syndrome, action myoclonus, cerebellar ataxia, post-hypoxic myoclonus, cardiorespiratory arrest

Introduction

The incidence of out-of-hospital cardiac arrest (OHCA) is estimated at approximately (37-121)/100,000 a year, and only 4.5% to 10.7% of patients survive to discharge [1]. Most survivors have increased sequelae due to ischemia anoxic encephalopathy (AIE), and present with post-hypoxic myoclonus (PHM) [1]. Two types of PHM can occur in patients: acute and chronic forms. Acute PHM emerges within the first 24 to 48 hours after cardiorespiratory arrest (CRA), and is associated with a poor prognosis. Chronic PHM, also known as Lance-Adams syndrome, is predominantly characterized by action myoclonus that starts days to weeks after cardiopulmonary resuscitation (CPR) in patients who regain consciousness [2, 3].

Accurate distinction between myoclonic status and LAS is important for initiating appropriate treatment early and for predicting the outcomes [4, 5]. Several studies have investigated the difference between the two forms of PHM, and revealed several differentiating clinical features, including time course, conscious level, presence of myoclonus, prognosis, and pathophysiology (Table 1) [2, 4, 6-9]. One well-established clinical feature to differentiate myoclonic status epilepticus (MSE) from LAS is consciousness. In the acute type of post-hypoxic seizures, the patient remains comatose, while in LAS, the patient later regains consciousness.

Another commonly used indicator is the PHM onset time. In acute PHM, myoclonus occurs within the first 24 to 48 hours after cardiorespiratory arrest, while in chronic PHM, myoclonus starts days or weeks after CPR. Electroencephalogram has also been proposed to distinguish LAS from acute PHM [2, 8]. Most LAS patients show epileptiform waves [2]. Elmer identified two distinct patterns of EEG to distinguish LAS and acute PHM; vertex spike-wave complexes (indicating Lance-Adams syndrome) and suppression-burst background with high...
amplitude spikes representing those previously described as “acute” PHM, with poor rates of survival [8].

Here we present an atypical case of LAS where the patient had generalized myoclonic movements 24 hours after the accident but then recovered consciousness about 1 month later. These features led us to misdiagnose the case as early-stage acute PHM.

### Case presentation

A 49-year-old woman without past medical history was admitted to our department in a coma. She was found in cardiac arrest following a work accident in which she was buried in mud for 10 minutes. After 5 minutes of CPR, her vital signs returned to the normal ranges while she remained comatose and intubated. A CT scan of the brain revealed no abnormalities.

| Table 1. Distinguishing features of myoclonic status epilepticus and Lance-Adams syndrome |
|---------------------------------|---------------------------------|
| **Conscious level** | Comatose | Aware, caution re sedation |
| **Time course** | Within 12-24 h, stopping after 24 hours | Later onset, may become chronic |
| **Myoclonus** | Generalized, multifocal | Usually intention myoclonus |
| **Prognosis** | Extremely poor | Normally preserved intellect, +/− chronic myoclonus |
| **Pathophysiology** | Ischemic brain injury with neuronal necrosis | Hypoxic brain injury without irreversible infarction |

Figure 1. T2-weighted and FLAIR images of brain magnetic resonance imaging showing increased signal intensity in the insular cortex and thalamus.
About 22 hours after admission, while still sedated, the patient had a tonic-clonic seizure, which ceased after 2 minutes following administration of 10 mg intravenous diazepam. Twenty-four hours after admission, generalized myoclonic movements were continuously observed in the face, trunk, and limbs, which were managed with continuous infusion of midazolam (4-7 mg per hour) and controlled transiently. After doses of sodium valproate (30 mg/kg, then 3×800 mg/d), levetiracetam (20 mg/kg, then 4×500 mg/d), phenobarbital (0.3 mg/d), lamotrigine (25 mg/d, then 200 mg/d), and carbamazepine (600 mg/d) were increased, the seizures were still uncontrolled, and the patient continued to exhibit intermittent jerky movements.

After propofol infusion was started, the seizure activity was somewhat controlled. On day 21 of hospitalization, brain magnetic resonance imaging (MRI) demonstrated increased signal intensity in the insular cortex and thalamus on T2-weighted and FLAIR images (Figure 1). On day 38 of hospitalization, she was transferred to the rehabilitation department, and her level of consciousness on the Glasgow Coma Scale (GCS) was 15. On day 39 of hospitalization, she was transferred back to the intensive care unit due to constant jerky movements. On day 50 of hospitalization, she fully recovered consciousness, had no hemiparesis, and was able to follow simple commands such as opening her mouth and stretching her tongue. Manual muscle tests showed that while her muscles in all four extremities had a Medical Research Council grade of 4, she could not speak. Further investigation, including searches of the medical literature, revealed she had ataxia, dysmetria, dysphagia, and dysarthria. The myoclonic jerks were aggravated by voluntary coordinated action and disappeared during sleep. The severity of the myoclonus was proportional to the precision of the task that was required.

Figure 2. Electroencephalogram (EEG) showing an alpha dominant background activity, low-amplitude beta waves, paroxysmal low-amplitude slow waves, and spike-wave discharges. Rate: 2 cm/s, amplitude: 100 μV/cm.

After 2 months of hospitalization, her electroencephalogram (EEG) showed cyclic epileptiform waves (Figure 2) and MRI demonstrated insular ischemic stroke. After 5 months of hospitalization, she was diagnosed with Lance-Adams syndrome according to clinical presentation and instrumental findings. Clonazepam was gradually added to control the myoclonic jerks. Once the symptoms of continuous myoc-
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Ionus were alleviated, a MRI demonstrated brain atrophy (Figure 3).

Her medications (including midazolam, lamotrigine, and carbamaze used to treat the myoclonus) were gradually reduced until only clonazepam (8 mg/d), sodium valproate (800 mg/d), and levetiracetam (1000 mg/d) were administered. Her mini-mental state examination (MMSE) score was 8, which indicated severe cognitive disabilities. Her Hamilton Depression Scale (HAMD) score was 25 and Hamilton Anxiety Scale (HAMA) score was 5; both scores indicated she had severe depression. During hospitalization, she underwent intensive gait and swallowing therapy as well as drug treatment. When she was discharged about 26 months after the CPR, she was able to sit on the bed, grab things, and say simple words, however she was unable to walk independently. Her cognition improved (MMSE score of 15).

Discussion

Lance-Adams syndrome (LAS) can be a rare and confusing complication for clinicians. Since MSE and LAS have very different prognoses, it is essential to distinguish MSE from LAS and to identify LAS early. Previously, these two forms of PHM were differentiated by the time of onset. However, Freund revealed that 20% of cases of LAS could be diagnosed within the first 48 hours after injury, further complicating the diagnosis of “acute” versus “chronic” PHM [7]. In some reports, myoclonus began as soon as the patient was weaned off sedation, indicating that sedation may delay PHM onset and challenges proper diagnosis [6].

In this report, a middle-aged woman presented with an atypical case of LAS. She developed myoclonus early and was finally diagnosed with LAS. This case demonstrated an exception to the currently widely accepted rules differentiating between the two types of PHM, and illustrates how an acute PHM might potentially convert to a chronic PHM through therapeutic treatment.

In the present case, a CT test at an early stage did not show any abnormality in the brain, which is in agreement with previous reports stating that CT or MRI scans of the brain are not helpful in the diagnosis of LAS. The patient had generalized myoclonic movements during the 24 hours after the accident, and recovered consciousness about 1 month later. The early onset of generalized myoclonic movements and the long period of comatose matched the criteria for an acute PHM [5-7], whereas the regaining of consciousness matched the criteria for LAS [5-7]. This clinical manifestation questioned the reliability of using onset time of generalized myoclonic movements as a differential indicator of PHM.

Physicians should be cautious and exercise patience when making a diagnosis at an early stage based only on the coma timeline, due to the long periods and late recovery of unconsciousness. The ability to diagnose LAS within the first 48 hours is low, as signs of awakening
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may be masked by sedation [2]. Our case further implies that acute PHM may convert to chronic PHM through chemotherapeutic treatment and patient care. Further investigation is required to fulfill the potential of our treatment and care plan prior to the regaining of consciousness.

Administering an electroencephalogram (EEG) to patients with PHM is important. Indeed, it may be used to identify the underlying EEG background rhythm, as well as detect and guide the treatment of seizures, gather prognostic information, and help define the regions and severity of brain injury. Correlations between electrophysiological status myoclonus, imaging status of myoclonus [8], and the EMG burst with myoclonic activity [2, 10] may determine damaged sites in the brain.

Elmer described two distinct patterns of EEG predicting disparate outcomes: vertex spike-wave complexes (signifying Lance-Adams syndrome), and suppression-burst background with high amplitude spikes representing those previously described as “acute” PHM, with poor rates of survival [2]. Our patient’s EEG showed cyclic epileptiform waves after 2 months of hospitalization, which is in agreement with the general observation that most LAS patients show epileptiform activity [2, 10]. However it did not match the predicted EEG pattern described by Elmer [8].

Although neurotransmitter serotonin (5-hydroxytryptophan; 5-HT), gamma aminobutyric acid (GABA), and death of Purkinje cells located in the paravermal and vermal areas are thought to be responsible for enhanced motor excitability and myoclonus [11, 12], the exact pathophysiology of LAS is still unclear.

Since there is no current guideline on drug treatment against this disease, options are limited and are often decided empirically. Frucht and Fahn found that clonazepam, valproate, and piracetam were effective in treating approximately 50% of the cases [13]. Indeed, levetiracetam, zonisamide, clonazepam, and valproate may be recommended as first-line agents of choice [14]. In our case, we used diazepam, propofol, midazolam, lamotrigine, carbamazep, clonazepam, valproate, and levetiracetam. Of these medications, clonazepam produced a dramatic therapeutic response in controlling post-hypoxic myoclonus.

We present a case of LAS that was an exception to the commonly used diagnosis criteria used to distinguish between the two types of PHM. PHM may be alleviated with chemotherapeutic treatment and patient care. Finally, it is probable that acute PHM converts into chronic PHM after certain treatment and patient care.

Disclosure of conflict of interest

None.

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