


CASE REPORT

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Overnight response to levetiracetam in Lance–Adams syndrome presenting 3 years after cardiac arrest

Mahmoud A. AbdelRazek^{1,5*} , Ahmed Marey², Ahmed Taha³, Scott J. Morin⁴, Alexander Brodski⁴ and Roohallah S. Mollashahi¹

Abstract

Background Lance–Adams syndrome (LAS), also known as chronic post-hypoxic myoclonus manifests as myoclonic movements of the face, limbs, or trunk following hypoxic brain injury, which may occur during respiratory failure or cardiac arrest.

Case presentation We present a case and provide a video of a patient who developed LAS 3 years after experiencing cardiac arrest, presenting with action-induced generalized myoclonus upon standing. The patient exhibited a significant response to levetiracetam. To the best of our knowledge, this is the first reported case of LAS with such a delayed onset following the initial hypoxic event.

Conclusion It is crucial for clinicians to be aware of this treatable condition and recognize that its onset may be delayed, occurring years after a hypoxic brain insult. This improved understanding will facilitate prompt diagnosis and effective management of LAS, ultimately enhancing patient outcomes.

Keywords Myoclonus, Post-anoxic, Hypoxic–ischemic encephalopathy cardiac arrest, Anoxic brain

Background

Generalized myoclonus following hypoxic brain injury was first reported by Swanson and colleagues in 1962 [1]. The disorder, later named Lance–Adams syndrome (LAS), was first described by James Lance and Raymond Adams in 1963 when they reported four cases where action myoclonus occurred in conscious patients within days to weeks after a successful cardiac resuscitation [2,

3]. Action myoclonus refers to involuntary muscle contractions that occur during voluntary movements. Myoclonus represents the briefest involuntary movement originating from the nervous system, rather than muscle stimulation [4]. It is non-specific and can be best categorized according to its etiological origin into physiological (sleep jerks, hiccup), essential (primary symptom, non-progressive), epileptic and secondary LAS [5].

LAS is characterized by the occurrence of repetitive, often rhythmic; generalized, focal, or multifocal; motor myoclonic movements involving the face, limbs, or trunk. It typically manifests within days to weeks after hypoxic brain insults, such as those resulting from cardiac arrest or respiratory failure, and is thought to stem from increased neuronal excitability after brain injury [6–8].

The term ‘chronic’ is used to differentiate LAS from the acute form, which classically presents within hours after the hypoxic event and is referred to as post-hypoxic myoclonic status epilepticus (MSE) [9].

*Correspondence:

Mahmoud A. AbdelRazek

Razek2@hotmail.com; mabdelrazek@mah.harvard.edu

¹ Department of Neurology, Mount Auburn Hospital, Harvard Medical School, 300 Mount Auburn St, Cambridge, MA 02138, USA

² Alexandria University, Alexandria, Egypt

³ Mallinckrodt Institute of Radiology, Washington University in St. Louis, St. Louis, MO, USA

⁴ Department of Medicine, Mount Auburn Hospital, Harvard Medical School, Cambridge, MA, USA

⁵ Massachusetts Institute of Technology, Cambridge, USA



In this case report, we present a unique instance of a 74-year-old man who developed LAS 3 years after experiencing a cardiac arrest. Notably, our patient showed an initial remarkable response to treatment with levetiracetam. We aim to highlight the clinical manifestation, treatment, and the response to levetiracetam observed in our patient.

Case presentation

In July 2019, a 74-year-old man with a history of cardiac arrest in August 2016 presented to our hospital with one month of progressive bilateral lower extremity shaking, ultimately leading to an inability to walk. A neurological exam revealed action-induced generalized myoclonus, predominately affecting the lower extremities and provoked by standing (Additional file 1: Video S1).

MRI of the brain, cervical and thoracic regions showed only remote juxtacortical white matter disease changes in the right and left parietal convexities, without acute stroke, mass or enhancing lesions. CSF proteins were mildly elevated at 70 mg/dL with no oligoclonal bands or increased cells present. Blood and CSF toxic and metabolic workups were unremarkable.

Initially suspecting orthostatic tremors, the patient was trialed on gabapentin; however, it was discontinued a week later when his tremors worsened and were found to be distinctly action-induced.

The patient was then started on levetiracetam (LEV) 1 g twice a day after an intravenous loading dose of 2 g for a diagnosis of action-induced myoclonus, most likely due to delayed-onset Lance–Adams syndrome (LAS). Remarkably, within 24 h, the patient experienced near-complete resolution of his myoclonus, as previously described in cases of post-hypoxic myoclonus [10].

Follow-up in the neurology clinic initially demonstrated sustained improvement of his gait and strength on levetiracetam, with well-controlled myoclonus. Later on, over 4 years of follow-up, he required increasing doses of levetiracetam and subsequently baclofen and other muscle relaxants. There has been less control of his myoclonus and progressive deconditioning of his strength due to reduced walking in avoidance of falls. Other anti-epileptics were trialed such as valproic acid and perampanel, unfortunately with little impact.

Continuous 1-day video electroencephalography (EEG) revealed that episodes of truncal and limb myoclonus do not show an ictal electrographic correlate, additionally there were findings of rare centrally predominant generalized periodic discharges with a triphasic morphology and a frequency of 1–1.5 Hz and nearly continuous background with periods of 1–2 s of attenuation. Importantly,

no electrographic seizures were observed despite clinical myoclonus.

A limitation of our report is the lack of a detailed neuropsychological testing. However, the major concern of an epilepsy disorder has been excluded via EEG.

New onset myoclonic epilepsy, without a prior history of epilepsy, has almost never been described to occur beyond the sixth decade of life [11, 12]. Toxic and infectious workups from blood and CSF were unrevealing in our patient.

Interestingly, in most reported cases of “chronic post-hypoxic myoclonus” or LAS, the myoclonus occurs days to weeks after the hypoxic event, and cases occurring years later have rarely been described [6, 13, 14].

To the best of our knowledge, this is the first reported case of LAS presenting with myoclonic symptoms 3 years after the initial hypoxic event. However, one report documented a case that initially showed LAS symptoms 4 days after cardiac arrest, which was then successfully treated but presented with LAS relapse 8 years after the first episode [11]. This suggests that LAS presentation can be delayed for years. The exact mechanism behind this late presentation is not entirely clear, however, slow recovery and re-organization of the brain, delayed neurochemical imbalances, and secondary mechanisms such as an infection or other pathological stressors interacting with the initial insult could play critical roles.

Myoclonic syndromes, especially post-hypoxic ones, typically show an adequate response to levetiracetam (LEV), as seen in our patient and others [10]. Valproic acid and clonazepam are also commonly used therapies [4, 15]. After reviewing over 100 cases of LAS, Frucht and Fahn found that valproic acid and piracetam were significantly effective in about 50% of patients [15].

The underlying pathophysiology of LAS is still not fully understood [12]. As LAS is believed to be a form of cortical myoclonus, there is presumably hyperexcitability of the corticospinal output, which can either be because of excessive excitatory or reduced inhibitory circuitry [4]. This may explain LAS's response to medications like valproic acid and clonazepam, which enhance gamma-amino-butyric acid (GABA) transmission, where GABA-ergic neurons are powerful sources of inhibition for pyramidal cortical circuitry [4]. GABA-ergic transmission is not a primary mechanism of LEV, thus its effect in LAS is more difficult to explain [16]. Other authors suggest that temporary cerebral hypoxia causes a permanent synaptic rearrangement of the neuronal networks involved in the pathogenesis of post-hypoxic myoclonus [17].

Conclusion

This exceptional case underscores the significance of acknowledging the impact of a remote hypoxic injury to the emergence of a new movement disorder. It emphasizes the remarkable enhancement in the patient's quality of life upon prompt identification and treatment of the underlying etiology. The prognosis of Lance–Adams syndrome (LAS) is favorable when timely intervention is provided [16]. However, without adequate awareness and understanding of the syndrome, managing LAS can be a formidable challenge.

Further research is warranted to elucidate the pathophysiology of LAS, identify optimal therapeutic agents, and expand our knowledge of its clinical presentation. By deepening our insights into this rare condition, clinicians can better detect and manage cases of LAS, ultimately improving patient outcomes and quality of life.

Abbreviations

LAS	Lance–Adams syndrome
MSE	Myoclonic status epilepticus
GABA	Gamma-aminobutyric acid
LEV	Levetiracetam
CSF	Cerebrospinal fluid
EEG	Electroencephalography

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s41983-023-00721-8>.

Additional file 1: Video S1. Initial generalized action-induced myoclonic jerks preventing proper ambulatory function, followed by response one day later to intravenous levetiracetam 2 g loading dose.

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Author contributions

MAA: writing of the first draft, writing of the final draft, overseeing manuscript production. AT: writing of the final draft. AM: writing of the final draft. SM: writing of the first draft, review, and critique. AB: review and critique. RSM: review and critique.

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Availability of data and materials

All data and images generated or analyzed during this case report are included in this article. Further enquiries can be directed to the corresponding author.

Declarations

Ethics approval and consent to participate

The authors confirm that the approval of an institutional review board was not required for this work. Informed consent was obtained. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

Consent for publication

Patient written informed consent was obtained for this case report.

Competing interests

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