JOURNAL OF COMMUNITY HOSPITAL INTERNAL MEDICINE PERSPECTIVES, 2017
VOL. 7, NO. 3, 182–184
https://doi.org/10.1080/20009666.2017.1340730

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CASE REPORT

Lance–Adams syndrome associated with cerebellar pathology

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ABSTRACT

Lance–Adams syndrome (LAS) is an uncommon neurological disorder characterized by the development of chronic post-hypoxic myoclonus. There are relatively few cases described following successful cardiopulmonary resuscitation. We report a patient who developed LAS 3 months after successful resuscitation. Cerebral imaging studies indicate that brain pathology in LAS patients is not uniform, suggesting that the pathophysiology of myoclonus may vary from patient to patient. Our patient adds to this etiological heterogeneity by demonstrating the unusual feature of cerebellar pathology by both cerebral magnetic resonance imaging and single-photon emission computed tomography scans. There is also heterogeneity of these patients in their response to therapy. Unlike some patients described in the literature, our patient has not responded to drug treatment. Studies of these rare patients with LAS are important as they provide insight into the pathophysiology of this condition which, it is hopefully, will facilitate the development of more effective therapy.

ARTICLE HISTORY
Received 27 January 2017
Accepted 26 May 2017

KEYWORDS
Lance–Adams syndrome; neurological complication; cardiopulmonary arrest; cerebellar lesion

1. Introduction

Cardiorespiratory arrest is a common occurrence, often leading to brain hypoxia, and is associated with high mortality and morbidity among survivors. Recent advances in cardiopulmonary resuscitation (CPR) training and intense post-resuscitation hospital care have improved survival rates [1]. However, survivors may develop a number of acute and chronic neurological complications including myoclonus. This is a neurological disorder characterized by sudden, involuntary jerky movements of a muscle or group of muscles precipitated by voluntary action and alleviated by rest and during sleep.

Post-hypoxic myoclonus (PHM) can develop acutely in a resuscitated patient who is usually in a coma. It typically develops within 48 h after a cardiac arrest and is termed post-hypoxic myoclonic status epilepticus (MSE) [2]. In contrast, there is a chronic form of PHM which was first described by Lance and Adams in 1963, in four patients. It was termed Lance–Adams syndrome (LAS) and is also known as chronic PHM. It is characterized by the development of action myoclonus in conscious patients days or weeks after a successful CPR [3]. Chronic PHM is rare and, as of 2011, fewer than 150 cases had been reported in the literature [4]. In most of the reported patients, chronic PHM developed following hypoxia in the setting of respiratory arrest associated with anesthetic or surgical accidents. In a few cases, it has also developed following cardiac arrest, drug intoxication, and asthmatic attack [5]. In this study, we report a patient who developed LAS 3 months after a successful resuscitation from cardiac arrest.

2. Case presentation

A 36-year-old woman developed cardiac arrest following cocaine overdose and was successfully resuscitated. She was intubated and remained comatose for 16 days. She had a complex medical history with multiple admissions for uncontrolled hypertension, diabetes mellitus, asthma, chronic kidney disease, recurrent pericardial effusions, chronic depression, and polysubstance abuse.

When the initial neurological examination was performed after CPR, the patient was intubated and non-responsive to verbal command. She withdrew all of her extremities to pain and had preserved brainstem reflexes. She was diffusely hyporeflexic with mute plantar reflexes. The overall assessment was consistent with hypoxic ischemic encephalopathy with a guarded prognosis. Remarkably, she regained consciousness 16 days later and slowly recovered with minimal residual cognitive impairment and was ultimately discharged to a rehabilitation facility. At discharge, her Mini-Mental Status Examination score was 27/30.

About 3 months later, she noted periodic involuntary movements of both arms and legs precipitated by action. Neurological examination disclosed that she

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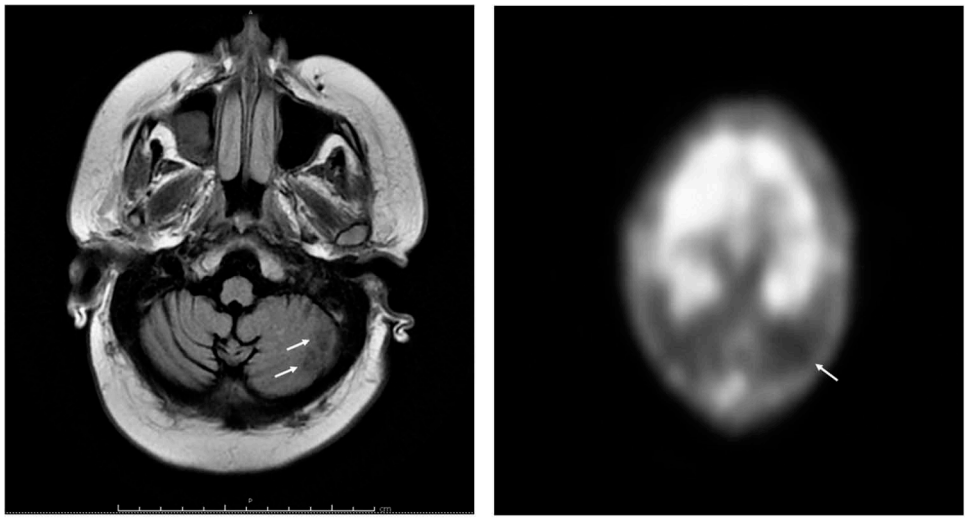

Figure 1. Cranial imaging studies following onset of myoclonus at 3 months post-cardiopulmonary resuscitation. (A) Coronal cranial magnetic resonance imaging without contrast showing chronic right cerebellar infarcts (arrows). (b) Brain single-photon emission computed tomography showing normal and symmetrical activity in the cerebral hemispheres and an area of decreased perfusion in the right cerebellum (arrow).

was alert and oriented to person, place, and time, and cooperative. She had a left central facial paresis and was dysarthric. Power testing showed normal strength in both proximal and distal musculature and she had hypoactive stretch reflexes with plantar extensor responses. She was unable to walk due to the myoclonus. Stimuli such as touch, sounds, and startles all triggered myoclonic jerks that disappeared with relaxation.

An electroencephalogram was performed and was normal with no evidence of paroxysmal activity suggestive of seizures. Cranial magnetic resonance imaging (MRI) showed multiple chronic cerebellar infarcts, larger on the right than the left (Figure 1 (a)). Brain single-photon emission computed tomography (SPECT) showed an area of decreased activity in the right cerebellum but was normal and symmetrical in the cerebrum (Figure 1(b)).

Based upon her clinical examination and investigations, LAS was diagnosed. She was treated sequentially with clonazepam 0.5 mg daily, divalproex sodium 250 mg twice daily, and baclofen 10 mg three times a day for 12 weeks, with no improvement of her symptoms. These were the maximal doses that she could tolerate for each medication prescribed without developing unacceptable side effects.

3. Discussion

The time of onset and clinical features in our patient are consistent with those described in the published cases of LAS.

Since this condition is rare, there are few studies specifically addressing the role of cerebral MRI in LAS. The largest reported review of cerebral MRI in LAS involves 12 patients in whom the imaging studies were performed after a mean of 2.5 years following the hypoxic event. In these patients, the MRI images showed no abnormalities in four patients, non-specific abnormalities such as mild cortical and cerebellar atrophy in four, and cerebral infarcts in three patients. In one patient, focal infarcts in the right cerebellar hemisphere were noted [6]. A serial MRI study evaluating LAS from the early stages showed early and transient involvement of the cerebellum and thalamus [4]. These authors propose that, in spite of the transient nature of this involvement, a permanent alteration in the neural networks is provoked, contributing to the pathophysiology of LAS. In our patient, the cerebral MRI showed multiple chronic bilateral cerebellar infarcts, which were more prominent on the right.

Recent studies have suggested that other imaging studies, such as cerebral SPECT scans or positron emission tomography (PET) scans, may provide some insight into disease pathophysiology. In a series of seven patients, PET scans showed an increase in glucose metabolism in the ventral lateral thalamus and pontine tegmentum [7]. However, this is not a consistent finding, as other reports have described a decrease in glucose metabolism in the frontal lobe [8]. Cerebral SPECT scans have been reported in three patients, with a decrease in perfusion in multiple regions including the basal ganglion, frontal lobe, parietal lobe, and left temporal lobe. However, the SPECT scan in our patient showed the unique finding of decreased perfusion in the region of the chronic right cerebellar infarct but with normal cerebral perfusion.

Initially, the pathophysiology of LAS was proposed to involve repetitive firing of the thalamocortical fibers arising from the ventrolateral nucleus of the thalamus, which is the main relay nucleus from the cerebellum to the sensorimotor cortex [3]. Only one other LAS patient has been previously described with a chronic cerebellar lesion by MRI studies [6]. Our case is the second report of a patient with LAS with MRI evidence of cerebellar pathology and the first with SPECT perfusion evidence of cerebellar dysfunction. In both these patients, it is possible that the cerebellar lesion initiated the process that ultimately resulted in the disruption of pathways linking the cerebellum to the thalamus, and causing LAS.

There is heterogeneity of MRI, PET, and SPECT scan findings, suggesting that the mechanism of myoclonus in LAS patients may also be heterogeneous. Our patient adds to the investigational variability of these patients by demonstrating the unusual feature of cerebellar pathology by both MRI and SPECT scans. In addition, our patient has not responded to any medications and, depending on her clinical course, we are considering recommending deep brain stimulation [7]. Perhaps the lack of response to any of the prescribed medications is a consequence of the pathophysiological heterogeneity that may exist in these patients. As the number of patients surviving CPR continues to rise, it is likely that more patients with LAS will be diagnosed. Further studies of patients with this rare condition may provide insight into the pathophysiology and more effective treatments.

Acknowledgements

We thank the patient and her family for cooperating with this study.

Authors' contributions

All authors contributed to initial drafts of this publication; RPG, AD, and LR revised later drafts. All authors reviewed and approved the final draft.

Disclosure statement

No potential conflict of interest was reported by the authors.

Ethics and consent

This case study was approved by the local institutional review board.

Funding

The authors have not received any funding or benefits from industry or elsewhere to conduct this study.

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