ANAESTHESIA, PAIN & INTENSIVE CARE
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ORIGINAL ARTICLE

Chronic post-hypoxic myoclonus in intensive care: Lance Adams Syndrome

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Received: 27 February 2019;
Reviewed: 28 February 2019;
Accepted: 19 March 2019

ABSTRACT

Aim: Posthypoxic myoclonus (PHM) is a rare myoclonus syndrome observed after cardiac arrest, is difficult to control and has no definitive diagnostic method. The pathophysiological mechanism of PHM, also known as Lance Adams Syndrome (LAS), is unknown and definitive treatment options are limited. The aim of this study was to present cases of LAS and the follow-up results of treatment following cardiopulmonary resuscitation (CPR) in our hospital.

Methodology: This study included patients followed up in the intensive care clinic of our hospital between May 2012 and January 2017 after CPR in the intensive care unit (ICU). A retrospective review was made of the record files of patients who were evaluated by the Neurology Department because of epileptic seizures.

Results: Evaluation was made of 19 patients with no history of epilepsy/antiepileptic drug use and treatment initiated by the Neurology Clinic for LAS. The patients comprised of 11 males (58%) and 8 females (42%) with a mean age of 55.89 ± 19.65 y for survivors and 61.50 ± 16.12 years for non-survivors. The mean length of hospital stay was 35 days for survivors and 17.5 days for non-survivors.

Outcomes were determined as, mortality in 10 cases, long-term care in 7, and discharge with recovery in 2. Sodium valproate was used in 4 patients and levetiracetam in 15. The 7 patients on long-term care were found to have been lost in the 3-month period after discharge.

Conclusions: In Lance Adams Syndrome the EEG may not provide any pathological clue or show epileptic changes. An early start to treatment can lead to better prognosis. It can be concluded that after CPR, myoclonic contractions can be reduced, and morbidity and mortality can improve with early diagnosis and early treatment.

Key words: Post-hypoxic myoclonus; Post resuscitation; Cardiopulmonary resuscitation; Lance Adams syndrome

Citation: Şeker YT, Sözer N. Chronic post-hypoxic myoclonus in intensive care: Lance Adams Syndrome. Anaesth. pain & intensive care 2019;23(1):33-36

INTRODUCTION

As a very rare myoclonus syndrome observed after cardiac arrest, which is difficult to control and with no definitive diagnostic method, posthypoxic myoclonus (PHM) is classified into two forms according to the time that it emerges. If it is seen in the first 12 hours of deep coma, it is defined as acute PHM, and if contractions develop days or weeks after cardiac arrest, it is described as chronic PHM. This form of chronic post-hypoxic myoclonus is also known as Lance Adams syndrome (LAS).

LAS was first defined in 1963 as a post-resuscitative complication with high mortality, resulting from cerebral hypoxia, which causes secondary myoclonic contractions.[1,2] There is no definitive protocol for treatment.

In the literature, levetiracetam, piracetam, valproic acid, and clonazepam treatments have been reported for acute chronic PHM or LAS.[3-7]

The aim of this study was to present the data of cases of LAS which were detected during monitoring in the intensive care unit after in-hospital cardiopulmonary resuscitation (CPR), and their follow-up.

METHODOLOGY

This study was conducted in the Department of Anesthesiology and Reanimation at Bakırköy Dr. Sadi Konuk Training and Research Hospital in

November 2018. Approval for the study was granted by the Local Ethics Committee (decision no: 2018-476, dated: 17.12.2018)

A retrospective examination was made of the files of patient records who experienced epileptic seizures in the Intensive Care Unit (ICU), after CPR between May 2012 and December 2018. Patient data were retrieved from the hospital electronic filing system (MetaVision, IMD Software Canada). The demographic data of patients, history of epilepsy and antiepileptic drug use, hospitalization periods (days), medications used in treatment, diagnostic method, and outcomes (death, recovery, patient under care) were recorded.

Patients who died within the first 24 hours were excluded from the study. Epileptic seizure caused by hypoxic encephalopathy was confirmed by cranial magnetic resonance imaging (MRI) and neurology clinical consultations, and therefore antiepileptic drug treatment was commenced.

Statistical analysis: Data obtained in the study were statistically analyzed using SPSS 24.0 software (IBM Corporation, Armonk, NY, USA). The Mann-Whitney U test with Monte Carlo results was applied when the Independent-Sample t- test was used in conjunction with the results of the quantitative data to be compared with the bootstrap outcomes. Quantitative variables were stated as mean ± standard deviation (SD), and median range (minimum-maximum) values, and categorical variables were shown as number (n) and percentage (%). A value of $p < 0.05$ was accepted as statistically significant.

RESULTS

A total of 2667 case files were scanned in the study period. In 192 post-CPR cases, it was recorded that an anti-epileptic drug was administered in the monitoring process in ICU. In cases where medical treatment was administered by the Neurology Clinic due to post-hypoxic myoclonus, no anti-epileptic drugs were used. Due to mortality in the first 24 hours, 2 cases were excluded from the study.

The 19 patients included in the study comprised 11 males (58%) and 8 females (42%). Male gender was statistically significant in the non-surviving patients. The mean age was 55.89 ± 19.65 y for survivors, and 61.50 ± 16.12 y for non-survivors.

Table 1: The demographic data of cases, and length of stay in hospital

Parameter		Non-survivors	Survivors	Total	p value
Gender [n (%)]	Male	9 (90)	3 (33.3)	12 (63.2)	0.020
	Female	1 (10)	6 (66.7)	7 (36.8)	
Age (y) (Mean ± SD)		61.50 ± 16.22	55.89 ± 19.65	58.84 ± 17.65	0.505
Length of stay in hospital (days) [Median (Min/Max)]		17.5 (2 / 60)	35 (11 / 50)	19 (2 / 60)	0.043

Independent t-test (Bootstrap) - Mann Whitney U-test (Monte Carlo) / SD = Standard Deviation - Min = Minimum - Max = Maximum, p < 0.05 statistical significance

Table 2: Anti-epileptic medications of the cases, discharge status, reason for CPR and where performed

Variable	N (%)
Antiepileptic medication	
Sodium valproate	4 (21,05)
Levetiracetam	15 (78.95)
Reasons for CPR	
Cardiac	16 (84.21)
Central Nervous System	2 (10. 53)
Trauma	1 (5.26)
Where CPR was applied	
Emergency Department	13 (68.32)
Coronary Intensive Care	5 (26.40)
Operating Theatre	1 (5.28)
Discharge Status	
Death	10 (52.63)
Care	7 (36.84)
Recovery	2 (10. 53)
Time of Onset of Seizure	
72 hours	10 (52.63)
3-7 days	6 (31.58)
7-14 days	3 (15.79)

The length of hospitalization ranged from 48 hours to 60 days. When the hospitalization period was examined, the earliest mortality was seen at 48 hours and the latest at 60 days. The length of hospital stay of survivors ranged from 11 days to 50 days. A statistically significant difference was determined between survivors and non-survivors in respect of length of stay in hospital and duration of intensive care ($p = 0.043$).

When the reasons for CPR were examined, 16 cases were due to cardiac causes, 2 cases were of central nervous system origin and 1 case was of trauma-induced cardiac arrest (Table 2).

Resuscitation was performed in the Emergency Department in 13 cases, 1 patient in the operating room and 5 in the Coronary Care Unit (CCU). The longest duration of resuscitation was 45 min (applied to 3 cases) and the shortest time was 10 min (applied to 5 cases). The mean resuscitation time

was 24.21 min. There was no statistically significant correlation between the duration of resuscitation and survival. Mortality was seen in 10 cases during treatment and follow-up in ICU, and 7 patients were discharged as patient under care with hypoxic encephalopathy (Table 2).

Two cases were discharged with recovery. Sodium valproate (Depakin© 500 mg tablet, Sanofi-Synthelabo, Turkey) was administered as antiepileptic agent in 4 cases, and levetiracetam (Keppra© 500 mg tablet, UCB Pharma) in 15.

When the time of onset of seizure was examined, myoclonic contractions were detected at 72 h in 10 cases. No pathology was detected on MRI of these cases. Myoclonic contractions were observed in the first week in 6 cases, and in the second week in 3, and these cases were identified as being consistent with acute cytotoxic edema on MRI (Table 2).

In the survivors, 90-day mortality and the presence of epileptic seizures were examined. Complaints were seen to continue after hospital discharge despite medical treatment. The 7 patients who were discharged as maintenance patients died within the 3-month period after discharge.

DISCUSSION

Due to diagnostic difficulties, post-hypoxic myoclonus is classified according to the time of emergence, so it is important that the possible etiological causes of myoclonic muscle are not overlooked.

The electroencephalographic (EEG) characteristics of this syndrome have not been reported in literature. In one case report of post-hypoxic myoclonus, the patient showed simultaneous contractions of multiple spikes following slow waves on electromyography (EMG) and EEG.[8]

However, in case reports, two-sided independent periodic lateralized epileptiform discharge (BIPLEDs) or myoclonic muscle movements showing a variable relationship, which may be spike wave activity, in addition to EEG results within normal boundaries, have been reported.[9,10]

In the current study patients, no bedside EEG was taken during contractions. On MRI used in diagnostic imaging of LAS, Wallerian degeneration, cerebral atrophy, and in some cases, no pathology can be detected.[11]

Hypoxic areas were detected on the cranial MRI and diffusion-weighted imaging of the current study patients. In LAS, cerebral spinal fluid (CSF) is assumed to have neurochemical and electrophysiological abnormalities.

Decreased serotonin efficacy in the inferior nuclei is thought to be one of the factors in the formation of LAS.[12] The 5-Hydroxyindol acetic acid levels seen in CSF may also be an example of such neurochemical abnormalities.[8]

The interaction of serotonin with gamma-aminobutyric acid (GABA) in cellular damage after hypoxia may be effective in inhibiting the myoclonus. Cerebellar ablation of GABAergic inhibition in afferent neurons may cause contractions by increasing the motor adaptability function.[13,14]

The causes of LAS are not exactly known. Therefore, the medication options that can be used to treat myoclonus are limited, but an earlier start is known to result in a better prognosis. As many neurotransmitters play a role in the pathophysiology of the disease, it can be understood why combination therapies yield better results.[15,16]

In patients who do not respond to other treatment options, it has been reported that combined or monotherapy with levetiracetam, which inhibits glutamate transmission, may be used in the treatment of post-hypoxic myoclonus.[5,6,17] In the current study, sodium valproate was administered to 4 patients and monotherapy with levetiracetam to 15.

The treatment of these cases was seen to be compatible with reports of monotherapy in literature. During the period of monitoring in ICU, 10 of the current study cases were lost, and a further 7 during the 3-months after discharge. The development of LAS was therefore concluded to have a negative impact on morbidity and mortality.

LIMITATIONS

A primary limitation of this study was the retrospective design. In addition, there were no EEG data as the facilities were not sufficient to enable testing on the patients. Diagnoses were made by clinical presentation and MRI interpretation only.

CONCLUSION

Lance Adams syndrome should be kept in mind for patients who develop focal or generalized myoclonic contractions in ICU following CPR. From the results of our study, it was concluded that early diagnosis and treatment of seizures with mono or combined therapy can reduce morbidity and mortality.

Conflict of interest:

This study received no external funding. Authors have no conflict of interests to declare.

Author contributions:

YTŞ: Conduct of study, designed, analyzed, and prepared manuscript

NS: Conduct and design the study, analyzed data, prepared manuscript

REFERENCES

1. Lance JW, Adams RD. The syndrome of intention or action myoclonus as a sequel to hypoxic encephalopathy. Brain. 1963 Mar;86:111-36 [PubMed]

2. Frucht S. Myoclonus. Curr Treat Options Neurol. 2000;2:231-42.

3. Wicklein EM, Schwendemann G. Use of clonazepam and valproate in patients with Lance Adams syndrome. J R Soc Med. 1993 Oct;86(10):618 [PubMed]

4. Söğüt A, Demir GA, Gökyiğit A, Çalışkan A. Lance-Adams sendromu: Klonazepamvevalproatkombinetedavisineiyicevap vermis¸ birolgu. NöropsikiyatriArşivi 1994;31:211-4.

5. Krauss GL, Bergin A, Kramer RE, Cho YW, Reich SG. Suppression of post-hypoxic and post-encephalitic myoclonus with levetiracetam. Neurology. 2001 Feb;56(3):411-2 [PubMed]

6. Venot M, Weiss N, Espinoza S, Imbert A, Tadie JM, Fagon JY, et al. Improvement of early diagnosed post-anoxic myoclonus with levetiracetam. Intensive Care Med. 2011 Jan;37(1):177-9. [PubMed]

7. Altunkaynak Y, Ertem DH, Köksal A, Yılmaz A, Baybaş S. Posthypoxicmyoclonic encephalopathy (Lance-Adams Syndrome): A case report. Parkinson HastalığıveHareketBozuklukları-Dergisi 20111;14(2):52-55

8. Hallett M, Chadwick D, Adam J, Marsden CD. Reticular reflex myoclonus: a physiological type of human post-hypoxic myoclonus. J Neurol Neurosurg Psychiatry. 1977 Mar;40(3):253-64 [PubMed] [Free Full text]

9. Wicklein EM, Schwendemann G. Use of clonazepam and valproate in patients with Lance Adams syndrome. J R Soc Med. 1993 Oct;86(10):618 [PubMed]

10. Saiz-Sepulveda MA, Garcia-Fernandez M, Martinez-Orozco FJ, Villalibre-Valderrey I, Jimenez-rucht F. Post-anoxic myoclonic encephalopathy (Lance-Adams syndrome) after prolonged cardiopulmonary resuscitation. Clin-Neurophysiol 2009;120:4:143

11. Venkatesan A, Frucht S. Movement disorders after resuscitation from cardiac arrest. Neurol Clin. 2006 Feb;24(1):123-32 [PubMed]

12. Welsh JP, Placantonakis DG, Warsetsky SI, Marquez RG, Bernstein L, Aicher SA. The serotonin hypothesis of myoclonus from the perspective of neuronal rhythmicity. Adv Neurol 2002;89:307-29 [PubMed]

13. Matsumoto RR, Truong DD, Nguyen KD, Dang AT, Hoang TT, et al. Involvement of GABA (A)receptors in myoclonus. Mov Disord 2000;15 Suppl 1:47-52 [PubMed]

14. Jaw SP, Nguyen B, Vuong QT, Trinh TA, Nguyen M, Truong DD. Effects of GABA uptake inhibitors on posthypoxic myoclonus in rats. Brain Res Bull. 1996;39(3):189-92 [PubMed]

15. Pappert EJ, Goetz CG. Treatment of myoclonus. Treatment of movement disorders. 1st ed. Philadelphia: Lippincott; 1995 pp

16. Werhahn KJ, Brown P, Thompson PD, Marsden CD. The clinical features and prognosis of chronic posthypoxic myoclonus. Mov Disord. 1997 Mar;12(2):216-20 [PubMed]

17. Frucht SJ, Louis ED, Chuang C, Fahn S. A pilot tolerability and efficacy study of levetiracetam in patients with chronic myoclonus. Neurology. 2001 Sep 25;57(6):1112-4 [PubMed]

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