

# A Case of Atypical Lance Adams Syndrome in Respiratory Failure Following Organophosphate Poisoning

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**Abstract:** *Chronic post hypoxic myoclonus (PHM) also termed Lance-Adams syndrome (LAS)<sup>1</sup> is a rare complication that occurs after successful cardiopulmonary resuscitation, in which myoclonus appears upon recovery from the severe hypoxic event usually after few days. To date, <150 cases have been reported. The following case describes an atypical variant of LAS, where the survivor of cardiac arrest and respiratory failure following organophosphate compound consumption who developed refractory generalized myoclonus within 1 hour of resuscitation but regained consciousness after 10 days. This is the first case of Lance Adams Syndrome described in case of organophosphate poisoning. The aim of this report is to help physicians to identify this variant of post hypoxic myoclonus early as it is consistently associated with better survival rates than myoclonic status epilepticus.*

## 1. Introduction

Myoclonus refers to sudden, shock-like, involuntary body movements that can occur in various patterns, i.e., focal, multifocal, or generalized. There are several conditions that can lead to myoclonus, and myoclonus can be classified according to clinical presentation/etiology, examination characteristics, or pathophysiology.<sup>2</sup> Almost 20% cardiac arrest survivors develop myoclonus.<sup>7</sup> Posthypoxic myoclonus (PHM) can present acutely, termed posthypoxic myoclonic status epilepticus (MSE), occurs soon after a hypoxic insult and showing generalized myoclonic jerks for more than 30 minutes in patients who are deeply comatose,<sup>3</sup> which implies a poor prognosis. MSE predicts death or permanent vegetative state in more than 90% of survivors.<sup>4</sup> However, another variant is chronic post hypoxic myoclonus/Lance Adams Syndrome (LAS) where the patient later regains consciousness and is associated with much better prognosis.<sup>5,6</sup> The patient described here was diagnosed with LAS following resuscitation from cardiac arrest.

## 2. Case Report

A 29-year-old male was brought by ambulance to GMC Aurangabad on 1<sup>st</sup> January 2020 with history of consumption of Monocil (monocrotophos, an Organophosphorus compound) in the morning. He was drowsy on arrival with GCS of 9. He displayed signs of OP compound toxicity like loose stools, excess salivation, spontaneous fasciculations and constricted pupils. His heart rate was 66 and auscultation revealed bilateral crepitations. He had consumed the poison following a domestic dispute. His past medical and surgical history was unrevealing. He was not on any long-term medications nor did he have any history of abnormal behavior or substance abuse.

Decontamination was started as per protocol and he was started on Atropine-Pralidoxime infusion. He deteriorated in the next 30 minutes developing tachypnea and neck muscle weakness. He was promptly intubated and shifted to MICU for mechanical ventilation. His GCS had deteriorated to 6.

On Day 5 of admission and mechanical ventilation, his GCS improved to 10 but he continued to display signs of

cholinergic toxicity despite atropine infusion. Later in the night, he experienced a generalized tonic clonic seizure and went into cardiac arrest. He attained normal sinus rhythm and saturation of 97% after 5 minutes of resuscitation. He developed myoclonic jerks about an hour after resuscitation which responded to IV lorazepam. His relatives took Discharge against Medical Advice the next day and took him to a Private hospital. He was admitted there for 8 days during which he continued to receive mechanical ventilation and underwent a tracheostomy. As per his family, he remained unconscious and his myoclonus worsened.

His family took Discharge against Medical Advice from that hospital and was readmitted to our hospital. He was shifted to MICU for further management. His GCS was 6 and plantars showed extensor response. Pupils were sluggishly reactive to light. Myoclonus was generalized for which he was given 16mg/day IV Lorazepam for 2 days. He continued to receive antibiotics for ventilator associated pneumonia.

On Day 17, he regained consciousness but was not following commands. Pupils were equal and normally reacting to light. Plantar response was flexor. IV Lorazepam was withdrawn. On Day 19, he was able to follow commands but remained confused and disoriented. Myoclonic jerks returned and responded to Propofol infusion. Atropine infusion was stopped on the same day.

Propofol was continued for 3 days with good symptom control although the patient remained sedated for most of the day. Propofol was withdrawn and he was started on Carbamazepine 400mg/day, Levetiracetam 1000mg/day and Clobazam 20mg/day were also started. Myoclonus did reduce in intensity but remained persistent throughout the day, exacerbated by action and minimal while asleep. Dysarthria was present. Metabolic profile did not show any abnormality.

Patient was able to follow commands and able to take oral sips. Myoclonus persisted despite improved cognitive status. Levetiracetam was increased to 2000mg/day and lacosamide 50mg/day were added after 4 days. As myoclonus remained resistant to previous drugs, clobazam was stopped and clonazepam started at 2mg/day. Lacosamide was stopped, and Valproate started at 400mg/day. Clonazepam raised to 4mg/day after 1 week.

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He was successfully weaned off mechanical ventilation and started on T piece ventilation by Day 33. He was successfully decannulated on day 40. Valproate was increased to 600mg/day and clonazepam to 8mg/day. He was able to walk with support and able to clothe himself at day 47. Dysarthria was persistent. He was discharged on day 49 on valproate 600mg/day, clonazepam 8mg/day and Levetiracetam 2000mg/day. He was referred for speech rehabilitation.

### 3. Discussion

The most common etiologies of hypoxia are respiratory arrest (especially in asthmatic), anesthetic and surgical accidents, cardiac diseases, and drug overdose.<sup>8</sup> As per The American Academy of Neurology (AAN)<sup>4</sup>, the predictors of poor prognosis after CPR are: Absent papillary light response or corneal reflexes at 72 hours, extensor or no motor response to pain at 72 hours, myoclonic status epilepticus (MSE), Bilateral absent cortical responses on somatosensory evoked potentials (SSEP) at 72 hours, Serum neuron-specific enolase (NSE) higher than 33 µg/L. MSE predicts death or permanent vegetative state (PVS) in more than 90% of survivors.

Acute PHM presents within 24 hours and episodes lasting more than 30 minutes are termed as Myoclonic Status Epilepticus. As per *Wijdicks et al* and *Hui et al*, MSE is associated with very poor prognosis.<sup>4,9</sup> Patients with acute PHM mostly remain comatose. The EEG in these patients often shows polyspikes or a burst suppression pattern. There are also reports of severe neurological injury at autopsy in patients who have suffered significant hypoxic injuries and developed MSE.<sup>4,10</sup>

In 1963, Lance and Adams described four patients who developed generalized myoclonus associated with dysmetria, dysarthria, and ataxia. They hypothesized that this set of symptoms observed after cardiac arrest was the result of cerebral hypoxia.<sup>1</sup> LAS can be generalized or multifocal and is intention and stimulus-induced.<sup>3,11</sup> LAS presents later than MSE, and though it can occur months to years following cardiac arrest and even within hours.<sup>12</sup> LAS is more commonly associated with respiratory arrest than a primary cardiac arrest. Other associated features are Epilepsy, dysarthria, gait disturbance, dementia, spasticity, and incontinence<sup>14,15</sup>

Anatomo-pathological study in two cases of PHM revealed diffuse neuronal degeneration in the neurons of the cortex, thalamus and subthalamic nuclei supporting Lance-Adams who stated that the myoclonus might be the result of repetitive firing of ventrolateral nucleus that is the principle relay nucleus from the cerebellum to the sensorimotor cortex. Loss of 5-HT (5-hydroxytryptophan) within the inferior olive has may contribute to pathology.<sup>16</sup> *Kaplan and Freund (2017)* suggest that LAS may be cortical although it could be subcortical as well.

*Werhan et al* reported that most patient had onset of myoclonus while still in coma.<sup>13</sup> Although the chief distinction between acute PHM and LAS is regaining of consciousness in the latter although this is not always apparent. A recent review published by *Kaplan and Freund (2017)*<sup>5</sup> proposed a clinical and electrophysiological differentiation between acute PHM and LAS (Fig 1), although these have not been validated. Diagnosis may be masked by sedation after resuscitation. Acute PHM may be converted to chronic PHM with early intervention.

	Myoclonic status epilepticus	Lance-Adams syndrome
<b>Clinical features</b>		
Body parts involved	Generalised or multifocal; trunk, trapezius, sternocleidomastoid, face, limbs; proximal and distal limb involved	Generalised, multifocal, or focal; limb involvement depends on cortical versus subcortical sources
Timing of onset	Rarely after 72 hours post-cardiac arrest	From hours to years following cardiac arrest
Length of duration	Days to weeks	Days to years
Response to treatment	Usually poor	Variable
Neurologic examination	Usually comatose	Comatose if sedated; awake, alert, and cognition may be relatively preserved
Mortality rate	90-100% of cases	Unclear given selection and survivorship bias, but in one retrospective study 50% of patients with similar EEG findings survived
Good neurologic outcome	Rare, may be more likely with multifocal versus generalised MSE	Common
Circumstances of cardiac arrest	Longer time to CPR, less bystander resuscitation, higher rates of nonshockable cardiac rhythm on presentation	Often primary respiratory arrest
Stimulus-sensitivity of myoclonus	Yes	Yes
Spontaneous myoclonus	Yes	Occasionally
Intention myoclonus	No	Yes
<b>Neurophysiological findings</b>		
EEG findings	Generalised epileptiform discharges and burst suppression, status epilepticus noted by intermittent or continuous spike-waves; lateralised periodic discharges and focal discharges are less common; over time burst suppression can evolved into generalised periodic discharges; diffuse slowing less common; alpha coma, particularly later after cardiac arrest	Epileptiform activity in up to one-third of cases often maximally or primarily at the vertex especially within hours after cardiac arrest, can have normal background activity; diffuse or focal slowing; up to 20% are normal
SSEP	Normal or absent; giant SSEP not consistently demonstrated; lacking thorough evaluation of multifocal PHM	Can demonstrate both giant and normal-sized SSEP
EEG-EMG polygraphy	Typically lacks jerk-locking; a thorough evaluation of multifocal PHM is lacking	Jerk-locking has been noted in roughly 60% of cases
Localisation	Subcortical, possibly cortical	Both subcortical and cortical

Figure 1

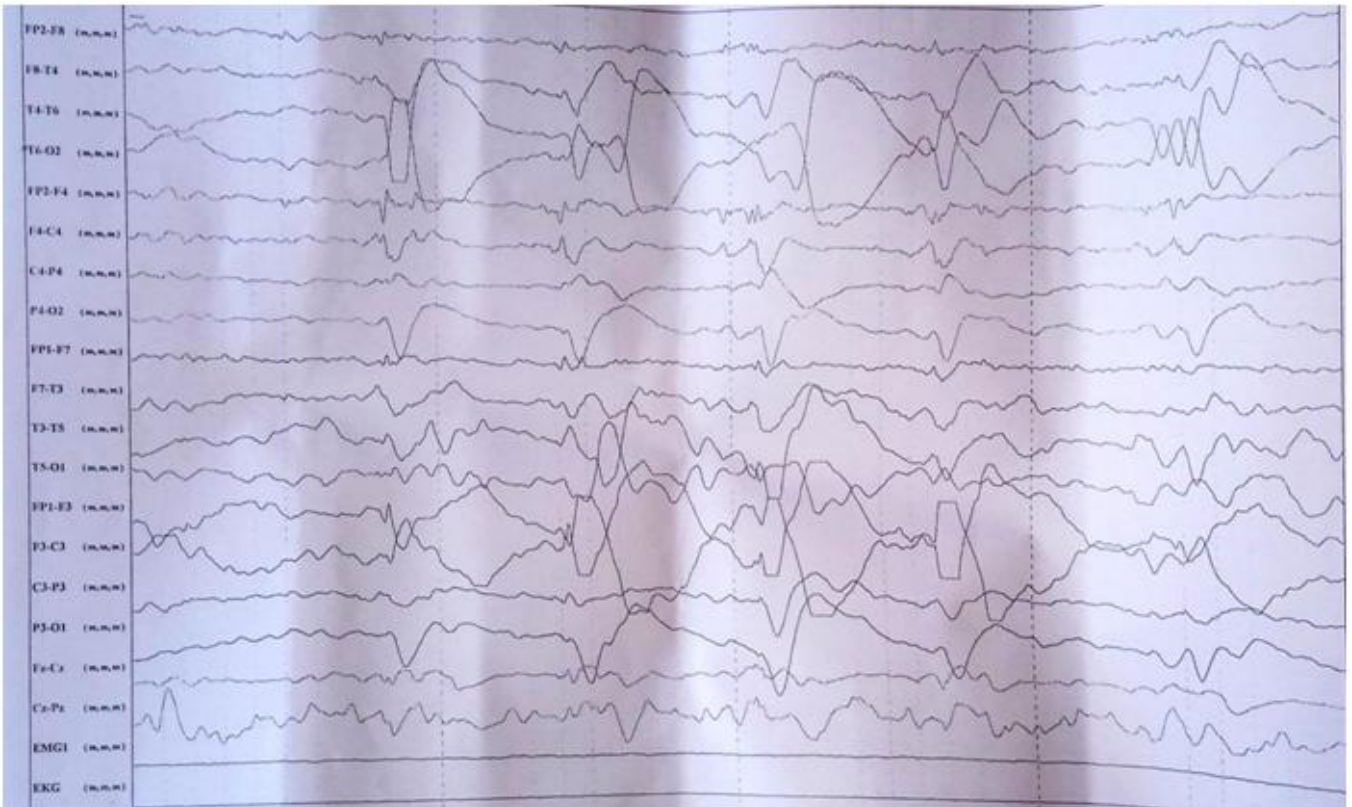
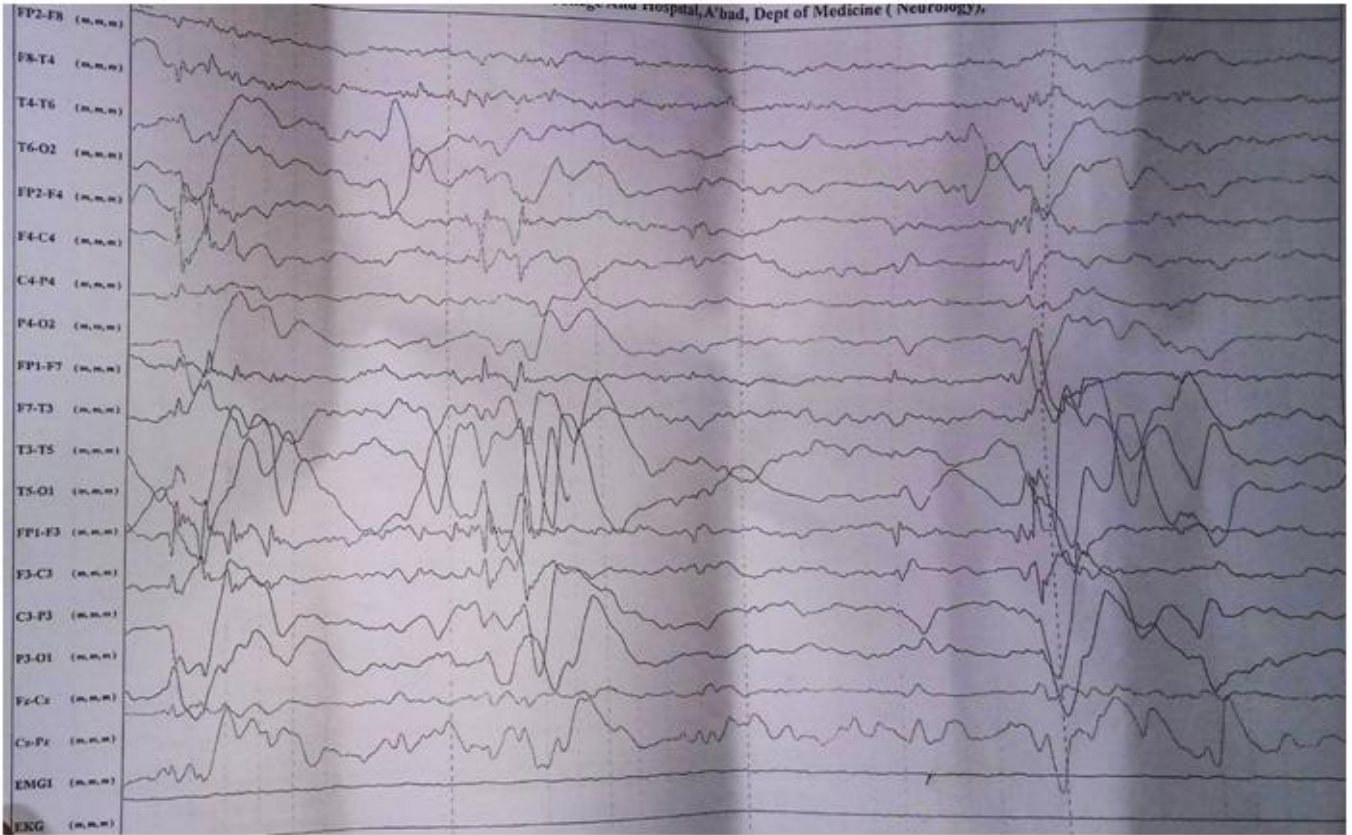
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Polyspike-wave discharges were noted primarily or maximally at the vertex. Some cases also demonstrated normal EEGs between myoclonic jerks.<sup>12</sup> Vertex-localized spike-waves on EEG 6–8 h after arrest may predict good prognosis and future diagnosis of LAS.<sup>17</sup> EEG changes may be nonspecific or even change over time.

EEG in our patient showed low voltage symmetrical theta waves in the background with spike and wave discharge waves over left and right fronto-central and left fronto-temporal region similar to EEG described by *Rittenberger*<sup>17</sup>.





Treatment of LAS is usually individualized as no controlled RCTs are available. Clonazepam, sodium valproate, piracetam, and levetiracetam have shown to be effective.<sup>18-23</sup> The prognosis had been reported to be good in LAS if early aggressive rehabilitation and appropriate drug treatment initiated. A review by *Frucht and Fahn (2000)* found more than 100 cases of LAS showing clonazepam, sodium valproate, and piracetam were significantly effective in approximately 50% of patients.<sup>24</sup>

#### 4. Conclusion

Post hypoxic myoclonus was traditionally associated with poor prognosis. This case report demonstrates that careful and detailed history taking, clinical examination and electrophysiological features as well patience is useful to make a diagnosis of Lance Adams Syndrome which is associated with better outcomes than myoclonus status epilepticus seen after hypoxic-ischemic cardiac arrest. It shows that early onset myoclonus after resuscitation might not necessarily lead to a fatal outcome. Early and aggressive treatment of myoclonus may convert Acute Post Hypoxic Myoclonus to Chronic Post Hypoxic Myoclonus. Difficulty in treating Lance Adams Syndrome also shows need for evidence-based guidelines and randomized controlled trials of treatment strategies.

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