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CASE REPORT

Myoclonus after cardiac arrest: pitfalls in diagnosis and prognosis*

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Summary

Accurate prediction of neurological outcome in survivors of cardiac arrest may be difficult. We report the case of a 44-year-old survivor of a hypoxic cardiac arrest who repeatedly developed relentless myoclonic jerks on attempted discontinuation of his propofol infusion. These were initially thought to represent myoclonic status epilepticus before the correct diagnosis of Lance–Adams syndrome was made. Lance–Adams syndrome is a rare disorder seen in survivors of profound hypoxic episodes. It is characterised by intention myoclonus but preserved intellect. Accurate distinction between myoclonic status epilepticus and Lance–Adams syndrome is vital as they have very different prognoses. The different pathophysiology and distinguishing clinical features of these two conditions are highlighted.

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Approximately 275 000 Europeans per year sustain emergency medical services (EMS) treated out-of-hospital cardiac arrest and about 5–10% survive to leave hospital [1, 2]. Survivors of cardiac arrest have a high incidence of neurological injury. A recent report from the Ontario Prehospital Advanced Life Support (OPALS) Study indicated that 12.5% of survivors of cardiac arrest had moderate or severe neurological impairment [3].

Accurate prediction of neurological outcome following cardiac arrest is important. False prediction of poor outcome may result in the patient being denied potentially life saving treatment. Over optimistic predictions of recovery may lead to ultimately futile prolongation of active medical treatment. Unfortunately accurate prediction of neurological function following cardiac arrest is difficult.

Many studies have investigated what factors predict poor neurological outcome following cardiac arrest [4–11]. Myoclonic status epilepticus at any time after return of spontaneous circulation (ROSC) is considered to reliably indicate a poor prognosis [7, 12, 13]. We present a case in which the incorrect diagnosis of myoclonic status epilepticus in this setting almost led to inappropriate withdrawal of active medical treatment. We review the evidence supporting myoclonic status epilepticus as a predictor of poor neurological outcome in patients following return of spontaneous circulation after cardiac arrest. The features that distinguish true myoclonic status from other forms of myoclonus, which importantly are not associated with universally poor neurological outcome, are highlighted.

Case report

A 44-year-old man presented to the emergency department with rapidly progressive head and neck swelling. This was associated with increasing respiratory distress. Relevant past medical history included morbid obesity (BMI 52) and hypertension. His only regular medication was losartan. A presumptive diagnosis of angioedema secondary to losartan was made. Intravenous access was established and he was given nebulised adrenaline (5 mg), intravenous hydrocortisone (200 mg) and intravenous

chlorphenamine (10 mg). Despite this treatment, he rapidly developed total airway obstruction. Orotracheal intubation was not possible because of airway swelling and an emergency surgical airway was therefore undertaken. This was technically difficult because of the patient's obesity and the extent of pre-tracheal oedema. The procedure was complicated by a cardiac arrest with pulseless electrical activity. Cardiopulmonary resuscitation was commenced immediately but adequate ventilation was not achieved until an emergency surgical airway was established. Return of spontaneous circulation occurred after 3 min of cardiac arrest. After exploration and repair of his neck wounds and oral intubation in theatre he was admitted to the intensive care unit (ICU). Sedation was maintained with propofol and alfentanil infusions and his lungs were mechanically ventilated whilst awaiting reduction of his airway swelling.

Twenty-two hours after admission, whilst still sedated, the patient had his first seizure. This was tonic-clonic in nature and was terminated after 2 min by intravenous lorazepam 2 mg. This was followed by an intravenous loading dose of phenytoin (1.5 g) and regular phenytoin (300 mg three times daily). Fifty-six hours after admission the first episode of myoclonic activity was reported. Sodium valproate 1 g twice daily and clonazepam 1 mg, as required, were commenced, whilst a propofol infusion was continued at 350 $mg.h^{-1}$. Seventy hours after admission, relentless myoclonic jerks were repeatedly observed within 2 min of stopping the patient's propofol infusion. At this stage withdrawal of active treatment was considered, but this was deferred until after an electroencephalogram (EEG) and neurology review were obtained.

Despite clinical evidence of myoclonic status whilst the patient was off sedation, an EEG performed at this time demonstrated frequent myoclonic polyspikes but did not confirm myoclonic status. A consultant neurologist advised that it was very difficult to be dogmatic about underlying cortical function whilst on so much sedation. Levetiracetam 1 g twice daily was started, sodium valproate was increased to 1.25 g twice daily and clonazepam was increased to 1 mg four times daily so that the propofol infusion could later be stopped to enable assessment of higher cortical function.

By day 5 of admission the propofol infusion had been stopped. Intermittent myoclonus persisted but purposeful movements were observed for the first time and the patient was intermittently obeying commands. The myoclonus was exacerbated by the patient attempting to perform tasks. This is known as intention myoclonus. Over the next 4 days the patient's conscious level continued to improve and the myoclonus reduced. Sadly, despite being successfully weaned from respiratory support by day 30 of his ICU admission and achieving a Glasgow Coma Score of 15, the patient did not survive to hospital discharge. He died of pneumonia 54 days after being admitted.

Discussion

Accurate prediction of neurological outcome following cardiac arrest is important. It is necessary to guide medical management and to guide discussion with the patient's relatives. In this case, the relentless myoclonic activity observed on attempted withdrawal of propofol sedation was initially mistaken for myoclonic status epilepticus. This could have precipitated withdrawal of active medical treatment and the premature death of the patient.

Despite the introduction of new diagnostic techniques, the most widely studied and reliable predictor of recovery of neurological function in those remaining comatose after cardiac arrest remains clinical neurological examination. In 2006, the American Academy of Neurology (AAN) produced evidence-based practice guidelines on the prediction of neurological outcome after cardiopulmonary resuscitation [7]. This group concluded that pupillary light response, corneal reflexes, motor responses to pain, myoclonic status epilepticus, serum neuron-specific enolase, and somatosensory evoked potential studies can assist in accurately predicting poor outcome in comatose patients after cardiopulmonary resuscitation. However, the limitation of myoclonic status epilepticus as a prognosticator is that it can be misdiagnosed [13–16]. In particular, it is important not to confuse it with the Lance–Adams syndrome, a separate clinical entity with a very different prognosis [17].

Myoclonic status epilepticus is defined as spontaneous, repetitive, unrelenting, generalised multifocal myoclonus involving the face, limbs and axial musculature in comatose patients. The clinical significance of myoclonic status epilepticus has previously been debated and some had questioned whether it was a potentially reversible epilpeptic phenomenon [18]. However in 1994 Wijdicks et al. [12] suggested that myoclonic status epilepticus in post-anoxic coma should be considered an agonal phenomenon that indicates devastating irreversible brain damage. They further suggested that its presence should strongly influence the decision to withdraw life support. They based these suggestions on the findings of their study of 107 consecutive patients who remained unconscious after admission to their hospital following resuscitation from cardiac arrest. Of the 107 patients, 40 had myoclonic status epilepticus on admission. Burst suppression was not universally present but was significantly more common in the myoclonus group when compared with those patients without myoclonic status (83% vs 7%). None of the 40 patients with myoclonic status survived; eight suffered from recurrent asystole or bradycardia

associated with refractory shock and in the remainder treatment was withdrawn. Postmortem examinations were performed in 15 patients with myoclonic status and 11 of the other patients. Cortical damage was significantly more severe in patients with myoclonic status. In addition multiple watershed infarcts were also more common in this group. The AAN practice guidelines reflect these findings [7]. In their meta-analysis they found that myoclonic status epilepticus in comatose patients on day 1 following cardiopulmonary arrest was associated with a false prediction rate for neurological recovery of 0% (95% CI: 0–8.8%). The authors also concluded that isolated seizures and sporadic focal myoclonus do not accurately predict poor outcome.

The patient in our review did not have myoclonic status epilepticus. He had developed Lance–Adams syndrome [17]. Fewer than 150 cases of this syndrome have been described worldwide and it has a very different prognosis from myoclonic status epilepticus. The distinguishing features of these two conditions are discussed below and summarised in the Table 1.

The single most important distinguishing feature between the two is the presence or absence of coma. Coma is a pre-requisite for the diagnosis of myoclonic status epilepticus. In contrast, patients with Lance–Adams syndrome are aware; however, the presence of sedation, as in this case, may mask awareness. Generalised multifocal myoclonus is seen in myoclonic status epilepticus whereas intention or action myoclonus predominates in Lance–Adams syndrome. Indeed intention or action myoclonus was the original term used by Lance and Adams to describe their syndrome in 1963. Despite these differences, there are no specific EEG changes in Lance–Adams syndrome that allow accurate distinction between myoclonic status and Lance–Adams syndrome in sedated patients (Personal communication: Dr N Kane, Consultant Neurophysiologist, Frenchay Hospital, Bristol, UK). Time from hypoxic insult to onset of myoclonic activity differs between the two conditions. Myoclonic status epilepticus usually presents within the first 12 h of insult and in most cases is no longer present after 48 h. Lance–Adams syndrome usually presents later and may run a chronic course [17].

The two conditions have very different prognoses. Whilst myoclonic status epilepticus is associated with a universally poor outcome, Lance–Adams syndrome is normally associated with survival with preserved intellect, with or without chronic myoclonus and cerebellar problems [14, 17, 19, 20]. The degree to which chronic intention myoclonus associated with Lance–Adams syndrome affects normal activities of daily living has been reported to vary, but amongst published cases there is a high proportion of patients who were unable to independently mobilise, wash, dress, feed themselves or return to work [14, 17]. The prognoses of the two conditions reflect the different underlying pathophysiology. Postmortem studies by Young et al. and Wijdicks et al. [12, 13] documented widespread ischaemic brain injury seen in myoclonic status epilepticus following cardiorespiratory arrest. In cases of Lance–Adams syndrome there is usually a documented period of hypoxia preceding hypoxic cardiac arrest, such as in cases of severe asthma or airway obstruction. The cerebral lesion in cardiac arrest following hypoxia has been shown to differ from that occurring in sudden circulatory arrest secondary to cardiac dysrhythmias [21, 22]. In hypoxic cardiac arrest, hypoxia induced metabolic changes produced by the primary period of severe hypoxia are thought to modify the cerebral lesion. The precise mechanisms for this hypoxic preconditioning are not known. Many factors have been suggested and it is likely that the hypoxic preconditioning involves many different substances [23–27].

Although the patient had not previously been diagnosed as having sleep-apnoea syndrome he had many of the common physical features associated with the condition. The presence of sleep-apnoea may have been of some relevance. Lavie et al. [28] hypothesised that the decline in mortality rates among patients with sleep-apnoea over the age of 50 years may be explained by cardiovascular and cerebrovascular protection conferred by ischaemic preconditioning resulting from nocturnal cycles of hypoxia-reoxygenation. This is a potential further mechanism whereby the patient may have been conferred some protection against the hypoxic insult suffered prior to and during his cardiac arrest.

In conclusion, it is important to recognise that post cardiac arrest myoclonus does not have a universally poor prognosis. It is vital to distinguish between myoclonic status epilepticus and the Lance–Adams syndrome.

Table 1 Distinguishing features of myoclonic status epilepticus and Lance–Adams syndrome.

	Myoclonic status	**Lance–Adams syndrome**
Conscious level	Comatose	Aware, caution re sedation
Time course	Within 12–24 h, stopping after 24 h	Later onset, may become chronic
Myoclonus	Generalised, multifocal	Usually intention myoclonus
Prognosis	Extremely poor	Normally preserved intellect, +/− chronic myoclonus
Pathophysiology	Ischaemic brain injury with neuronal necrosis	Hypoxic brain injury without irreversible infarction

Despite publications outlining the features of the Lance–Adams syndrome [14, 19, 20, 29, 30], our impression is that knowledge of this condition among critical care doctors remains poor. The key feature to help accurate distinction between these two clinical entities, which have very different pathophysiology and prognoses, is the presence or absence of coma. Importantly, this cannot be reliably assessed if patients remain on large doses of sedatives. The diagnosis of myoclonic status epilepticus, which is associated with a universally poor neurological outcome, must not be made unless patients remain comatose after sedatives have been eliminated.

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