Difficulties with neurological prognostication in a young woman with delayed-onset generalised status myoclonus after cardiac arrest due to acute severe asthma

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Abstract

Neurological prognostication in cardiac arrest survivors is difficult, especially when the primary etiology is respiratory arrest. Prognostic factors designed to have zero false-positive rates to robustly confirm poor outcome are usually inadequate to rule out poor outcomes (i.e., high specificity and low sensitivity). One of the least understood prognosticators is generalised status myoclonus (GSM), with case reports confusing GSM, isolated myoclonic jerks and post-hypoxic intention myoclonus (Lance Adams syndrome [LAS]). With several prognostic indicators (including status myoclonus) having been validated in the pre-hypothermia era, their current relevance is debatable. New modalities such as brain magnetic resonance imaging (MRI) and continuous electroencephalography are being evaluated. We describe here a pregnant woman resuscitated from a cardiac arrest due to acute severe asthma, and an inability to reach a consensus based on published guidelines, with a brief overview of myoclonus, LAS and the role of MRI brain in assisting prognostication.

Keywords: Generalised myoclonus, hypoxic encephalopathy, Lance Adam syndrome, MRI, neurological prognostication

Introduction

Unconscious survivors of ventricular fibrillation cardiac arrest in intensive care units (ICUs) are increasing. Neurological prognostication is difficult. Usually, patients who awaken do so within 48 h of stopping sedation; patients unconscious at day 7 remain severely impaired.[1] The current guidelines from studies in the pre-hypothermia era are often inadequate.[2] Specifically, the significance of myoclonus continues to be debated, especially following primary respiratory causes of cardiac arrest. We describe the difficulties with the timing and method of neurological prognostication in a comatose cardiac arrest survivor.

Case Report

A 28-year-old woman, 8 weeks pregnant, developed acute severe asthma, with a short non-infective prodrome, and a hypoxic cardiac arrest. Her initial rhythm in the emergency department was ventricular fibrillation. Resuscitation to sinus tachycardia required 10 min, including endotracheal intubation. On transfer to the ICU, she was therapeutically cooled to 33°C for 24 h.

Management included salbutamol (inhaled and intravenous), ipratropium, aminophylline, hydrocortisone, magnesium, ketamine and inhalation anesthesia with 1 MAC isoflurane. Severe hypercapnic acidosis from inadequate minute ventilation required neuromuscular blockade (NMB). With ventilation improving over 48 h, we intentionally ceased the intravenous sedatives and NMB, and used 0.25–0.5 MAC isoflurane as the sole sedative to avoid residual sedation from long-acting intravenous agents and facilitate early neurological assessment.
She developed generalised status myoclonus (GSM) by 48 h, when the neuromuscular blockers were stopped. When isoflurane was stopped on day 4, she was comatose, with absent motor response to painful stimulus, preserved pupillary, corneal, cough and gag reflexes and spontaneously breathing, with severe GSM, refractory to three antiepileptic medications. Electroencephalography showed generalised periodic discharges with no discernable background rhythm. Reversible causes of coma (biochemical, metabolic, septic and drugs) were eliminated by clinical examination, specific investigations and duration of action of sedative medications.

By day 8, there was no agreement about her neurological outcome among the clinicians. Additional social issues due to the interethnic marriage and the pregnancy required intensive social work support to help a disparate family understand the complicated process of neurological prognostication.

GSM (despite delayed onset at 48 h) was interpreted by some as a poor prognostic marker in a deeply comatose patient and by others as possible Lance Adams Syndrome (LAS) in the setting of a respiratory cause of cardiac arrest. The plasma neuron-specific enolase (NSE) was 51 mcg/L (indicating poor prognosis), but the results were delayed by 10 days. Somatosensory-evoked potential (SSEP) was unhelpful due to myoclonus motion artefacts.

On day 10, brain magnetic resonance imaging (MRI) using fluid attenuation inversion recovery and diffusion weighted imaging (DWI) was performed, which showed bilateral basal ganglia and frontoparietal cortex infarction “consistent with severe hypoxic encephalopathy” [Figure 1].

Medical consensus regarding poor prognosis was finally reached following discussions between two intensivists and two neurologists. She was extubated with family agreement, and died in 24 h with comfort measures.

**Discussion**

Neurological prognostication in post-anoxic survivors is difficult. The American Academy of Neurology (AAN) recommends:

- Eliminate reversible causes of coma
- Perform tests with zero false-positive rates to rule out poor neurological outcome
  - Day 1: GSM in primary circulatory arrest
  - Days 1–3: Bilateral absent N20 response on SSEP or NSE >33 mcg/L
  - Day 3: Absent corneal and pupillary reflexes and flexor motor response or worse to pain at 72 h

As predictors of poor neurological outcome, all the AAN prognostic indicators have limitations, the most important being the poor sensitivity of a “normal test.” A large proportion of comatose patients with no abnormalities still have a poor neurological outcome. A study in cardiac arrest survivors demonstrated that intravenous sedation for therapeutic hypothermia confounds the sensitivity of routine prognostic indicators such as corneal reflex, motor response and NSE. Our sedation management avoided this confounding effect.

Additional limitations are delays with NSE results, motion artefacts with SSEP and three specific issues with myoclonus:

- Delayed GSM: Pre-hypothermia era studies established Day 1 GSM as a poor prognosticator. Recent reports after hypothermia suggest that even early GSM may not reflect poor prognosis.
- Post-anoxic intention myoclonus in conscious patients (LAS) is a separate entity. By definition, these patients are awake (i.e., good neurological outcome) and display focal myoclonus brought on by the intention of moving a limb. It is mostly seen in anoxia from respiratory arrest and has been mistaken for status myoclonus in such settings.
- Residual sedation and myoclonus: One report of a patient with a respiratory arrest who “woke up” after...
“generalised” or even sporadic myoclonus doubted its prognostic value in this setting. This report was flawed, describing a patient who was deeply sedated to facilitate mechanical ventilation, who probably developed intention myoclonus under residual sedation while awakening. GSM is bilateral, involves face and limbs and persistent. Myoclonic patterns not fitting this description are not GSM by definition and do not have a prognostic value.

Most patients need additional but less-proven investigations, the most promising emerging modality being MRI brain. An abnormal MRI with multilobar, or diffuse, cortical involvement, termed as “extensive cortical lesion pattern” or extensive basal ganglia abnormalities, may have a reliable poor prognostic value with the above-mentioned limitation of poor sensitivity. Although the AAN guidelines considered MRI to have inadequate evidence as a prognostic tool, the evidence is growing.

The AAN indicators were unhelpful in our patient, with preserved brainstem reflexes and delayed GSM. Although the NSE was high, clinicians were uncomfortable using this sole test to prognosticate. Finally, LAS was wrongly considered “because of a respiratory aetiology,” although LAS only occurs when awake, and is not peculiar to respiratory arrest.

This case highlights the confounding factors of induced hypothermia with the AAN guidelines and delayed myoclonus, the need to avoid long-acting sedation, particularly in respiratory arrest, and the emerging role of MRI.

Our future policy for similar patients is to avoid long-acting sedatives whenever possible, use the AAN guidelines, but use MRI in complicated cases. Systematic studies on myoclonus in the hypothermia era and MRI are required.

Acknowledgment

The authors would like to acknowledge the help of Dr. Mark Thieben, Staff Specialist, Department of Neurology, Nepean Hospital.

References


How to cite this article: Rajamani A, Seppelt I, Bourne J. Difficulties with neurological prognostication in a young woman with delayed-onset generalised status myoclonus after cardiac arrest due to acute severe asthma. Indian J Crit Care Med 2011;15:137-9.

Source of Support: Nil, Conflict of Interest: None declared.