

Post-hypoxic myoclonic status: the prognosis is not always hopeless

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The early development of generalised, repetitive myoclonic jerks — myoclonic status — after cardiac arrest is associated with a poor prognosis, and some argue an invariably fatal outcome.^{1,2} However, several case reports have described neurological recovery in such patients.^{3,4} We describe a further case of dramatic neurological improvement in a patient with myoclonic status after cardiac arrest.

Clinical record

A 67-year-old woman of European ancestry underwent elective open-mesh repair of an incisional hernia at the site of a previous open cholecystectomy. Relevant past medical history included atypical chest pains, which were thought to be non-cardiac based on a preoperative thallium scan that gave normal results, and a transthoracic echocardiography that showed only mild aortic stenosis.

During the sixth postoperative night, the patient experienced an episode of acute chest pain and dyspnoea. Oxygen saturation by pulse oximetry dropped to 80%, and she became unresponsive, with a score on the Glasgow Coma Scale (GCS) of 3. Medical staff were present when her pulse became undetectable, while the electrocardiogram showed sinus bradycardia (pulseless electrical activity). She received 3 minutes of cardiopulmonary resuscitation before spontaneous circulation returned. She was intubated and transferred to the intensive care unit where she was found to have pulmonary oedema.

In the ICU, the patient was sedated with propofol and morphine, and mechanically ventilated with positive end-expiratory pressure until the pulmonary oedema resolved. Hypothermic brain preservation strategies were not used because of the brief period of cardiac arrest and initial cardiac instability. Six hours after admission to the ICU (ICU Day 1), the dose of propofol was reduced, and unrelenting generalised myoclonic jerks were observed. Midazolam was started in lieu of propofol in an attempt to control these. An infusion of vecuronium was also used intermittently to modify the severity of myoclonus and prevent hyperpyrexia. Intravenous phenytoin failed to alter the frequency or severity of the myoclonic jerks, which returned whenever sedation and muscle relaxation were reduced. The patient remained unconscious (GCS, 3), even when sedation was weaned.

On ICU Day 3, because of unremitting, generalised spontaneous myoclonus, enteral administration of the anti-epileptic

ABSTRACT

A 67-year-old woman abruptly developed acute pulmonary oedema, severe bradycardia and then cardiac arrest while in hospital 6 days after an elective hernia repair. She was resuscitated, intubated and transferred to the intensive care unit. Within 24 hours, she began to display repetitive, generalised myoclonic jerks that failed to respond to therapy with conventional anticonvulsants; an electroencephalogram confirmed myoclonic status. After administration of levetiracetam was begun on Day 3, myoclonic jerks reduced, and there was gradual clinical improvement. By Day 6 after the arrest, the patient was alert and oriented (Glasgow Coma Score, 15/15). Although she died on Day 11 after massive haemoptysis and cardiac arrest, this patient demonstrates the possibility of reasonable neurological recovery despite early onset of myoclonic status.

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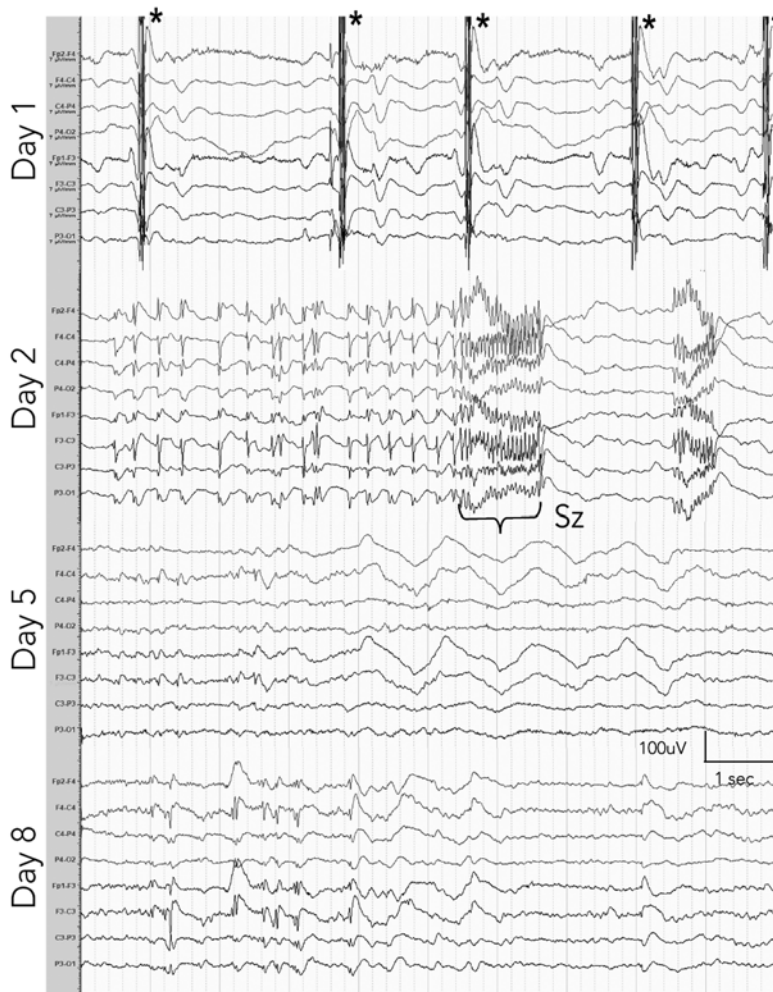
drug levetiracetam was begun. Over the next 12 hours, myoclonic jerks reduced but continued, particularly on auditory or touch stimulation. On Day 5 after the cardiac arrest, following a reduction in sedation, the patient appeared to be visually scanning the environment appropriately, despite ongoing intermittent generalised myoclonic jerks. On the morning of Day 6, she responded appropriately to verbal commands (GCS, 10T), although occasional myoclonic jerks localised to the left shoulder were still noted. Two days later, on extubation, she was able to converse with her family, was fully oriented (GCS, 15/15) and was able to feed herself, although with variable myoclonus localised to the left shoulder.

The patient was discharged to the general ward on Day 9, but was readmitted to the ICU because of recurrent acute pulmonary oedema. Two days later, she died after an episode of massive haemoptysis and cardiac arrest. An autopsy found severe coronary artery disease as the likely cause of death.

The appearance of the electroencephalogram (EEG) evolved during the patient's admission in parallel with the clinical picture (Figure 1). On ICU Day 1, the EEG was diffusely slow, consistent with hypoxic encephalopathy, and was regularly disrupted by high-amplitude muscle artefacts from myoclonic jerks. Although no epileptiform activity was evident, this was

Figure 1. Representative 10-second epochs of the electroencephalogram in a 67-year-old woman with post-hypoxic myoclonic status

All traces of the electroencephalogram (EEG) are at the same gain, and display the parasagittal traces from a standard bipolar montage in the international 10–20 system. Traces are (top to bottom): frontopolar–frontal, frontal–central, central–parietal, and parietal–occipital for right scalp; the same sequence for left scalp.



On Day 1 after hypoxia, the EEG was diffusely slow and disrupted by high amplitude muscle artefacts (*) caused by repetitive generalised myoclonic jerks.

On Day 2, with the patient paralysed by vecuronium, the EEG showed almost continuous generalised sharp and slow epileptiform activity at 2.5–4 Hz, disrupted by bursts of generalised polyspike consistent with electrographic seizures (Sz), followed by a brief period of flattening of the trace.

On Day 5, after 2 days of levetiracetam administration, myoclonic jerks had almost resolved, and the EEG showed sporadic generalised epileptiform discharges and moderate diffuse slowing.

On Day 8, with the patient able to converse, background EEG slowing was much less prominent. Sporadic generalised epileptiform discharges persisted, with variable myoclonic jerks localised to the left shoulder.

possibly obscured by the muscle artefacts. By Day 2, while the patient was receiving muscle relaxants, almost continuous generalised epileptiform activity was seen at a frequency of about 4 Hz, disrupted only by brief electrographic seizures, followed by a short period of relative EEG normalisation. By Day 5, the EEG showed a reduction in generalised epileptiform activity, with electrographic seizures no longer evident. This corresponded to the abolition of myoclonic jerks and improving cognition. By Day 8, improved background rhythms were apparent, at a frequency in the alfa–theta range (7–8 Hz).

Discussion

The development of the persistent, generalised jerking of myoclonic status soon after resuscitation after cardiac arrest has been considered an extremely grim prognostic sign. In a

series of 107 patients who remained comatose after cardiac arrest, none of 40 who were in myoclonic status improved neurologically or survived.¹ Myoclonic status can begin within 12 hours of arrest and may resolve within 48 hours, but is characteristically resistant to therapy.⁵ Some suggest that myoclonic status is an index of the severity of the initial hypoxic insult, and that aggressive treatment of seizures may not be warranted.^{6,7}

Myoclonic status should be distinguished from Lance–Adams syndrome, which usually refers to the delayed development of sporadic, often multifocal, movement-exacerbated myoclonic jerks several days after cerebral hypoxia.⁸ This may be associated with a favourable neurological outcome. Interestingly, the original report of this syndrome⁸ described patients who exhibited generalised myoclonus within 24

hours of the hypoxic event, which then lost its rhythmic character and became more localised within 2–4 days, accompanied by an improvement in neurological status.

Although myoclonic status is an adverse prognostic sign, its significance in individual patients remains uncertain. Observational studies are susceptible to bias, such as the possibility that the perceived poor prognosis of myoclonic status may have influenced decisions to withdraw treatment. In addition, there are several case reports of patients with a clinical picture consistent with post-hypoxic myoclonic status who made a good functional recovery. A recent retrospective review of patients with post-hypoxic status epilepticus, defined using EEG rather than clinical criteria, described three out of 35 surviving, one with a good neurological outcome.⁹ Our report adds to the literature suggesting that neither the early development of generalised myoclonic jerks (myoclonic status), nor the presence of recurrent generalised epileptiform activity on EEG should necessarily be considered a marker of severe irreversible brain injury.

As well as persistent generalised spike and slow wave epileptiform activity on Day 3 (Figure 1), our patient's EEG showed recurrent bursts of polyspike, consistent with brief electrographic seizures. We speculate that reduction of the persistent spike and wave discharges, or abolition of polyspike seizures may have contributed to improvements in her cognition. We do not consider our patient's EEG demonstrated "burst suppression", as described in some previous cases of myoclonic status, but acknowledge that differentiating recurrent electrographic seizures with post-seizure suppression from burst suppression can be difficult.

Although well described previously, the discordance between the clinical and electrographic epileptic features is curious. On Day 1, the patient had myoclonic jerks but no detectable epileptic activity on the EEG. On Day 5 and Day 8, with the patient no longer paralysed, generalised epileptiform discharges continued sporadically but were not associated with jerks. This is a reminder that the clinical and electrographic features of epileptic activity may be poorly correlated, especially after hypoxia.

Standard anti-epileptic drugs have been shown to have poor efficacy in post-hypoxic myoclonus,¹⁰ as observed in our patient, who had minimal benefit from phenytoin or the benzodiazepine, midazolam. Levetiracetam has been shown to be beneficial in partial epilepsy, as well as various myoclonic epilepsies.^{11,12} Although our patient's myoclonic jerks abated, and clinical improvement began, around the time levetiracetam began, to be administered, it remains possible that this occurred independently of the drug.

The full mechanism of action of levetiracetam is not entirely known. In-vitro studies show reduced intraneuronal release of calcium ions and partial inhibition of γ -aminobutyric acid and glycine-gated currents. Animal studies have shown a possible anticonvulsant mechanism via binding to synaptic vesicle

protein 2A, thought to be involved in neurotransmitter vesicle fusion and exocytosis.¹³ The drug has a linear dose–response profile, with oral bioavailability close to 100%. There are no known interactions with anti-epileptic or other drugs. Excretion is predominantly renal.

While myoclonic status remains a poor prognostic sign, and our patient's ultimate neurological outcome, had she survived, is unknown, the case suggests that a reasonable neurological outcome is possible. In individual patients with post-hypoxic myoclonic status, a trial of levetiracetam to reduce myoclonic activity may be warranted. However, to determine whether this drug truly affects outcome of post-hypoxic myoclonic status, a controlled trial would be needed.

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