Neurological Prognostication of Cardiac Arrest in an Era of Extracorporeal Membrane Oxygenation

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Abstract

A neuron-specific enolase level greater than 33 ng/mL at days 1 to 3 or status myoclonus within 1 day are traditional indicators of poor neurological prognosis in survivors of cardiac arrest. We report the case of a 70-year-old man who received extracorporeal membrane oxygenation following cardiac arrest. Despite having both an elevated neuron-specific enolase concentration of 68 ng/mL and status myoclonus, he made an excellent neurological recovery. The value of traditional markers of poor prognosis such as elevated neuron-specific enolase or status myoclonus has not been systematically validated in patients treated with extracorporeal membrane oxygenation or therapeutic hypothermia. Straightforward application of practice guidelines in these cases may result in tragic outcomes. This case underscores the need for reliable prognostic markers that account for recent advances in cardiopulmonary and neurological therapies.

Keywords

neurocritical care, clinical specialty, prognosis, coma, neuron-specific enolase, status myoclonus

Introduction

Elevated serum neuron-specific enolase (NSE) concentrations and generalized myoclonus are considered poor prognostic markers after cardiac arrest.¹ Neuron-specific enolase is the neuronal form of the intracytoplasmic glycolytic enzyme enolase and is widely used to detect neuronal injury. Despite its name, NSE is also found within red blood cells.^{2,3} Generalized myoclonus or “status myoclonus” is characterized by involuntary, multifocal, and sustained twitching of the face, limbs, and axial musculature in the presence of coma. No specific electroencephalogram pattern is required to make the diagnosis; voltage attenuation, burst suppression, epileptiform discharges, and electrographic status epilepticus patterns have all been reported in association with status myoclonus.² Status myoclonus should be differentiated from posthypoxic myoclonus, or Lance-Adams syndrome, which may occur following primary respiratory arrest and be associated with a more favorable neurological prognosis.^{4,5}

The prognostic utilities of NSE or status myoclonus have not been validated in patients who receive mechanical circulatory support such as those with extracorporeal membrane oxygenation (ECMO). This case reports a patient who was resuscitated after cardiac arrest and received ECMO. He had

an excellent neurological recovery, despite demonstrating both markedly elevated NSE levels and status myoclonus. In addition to informed consent from the patient’s next of kin, institutional review board approval was obtained for publication of this case report and accompanying images.

Case

A 70-year-old man with extensive cardiac history including ischemic cardiomyopathy and bicuspid aortic valve requiring 4-vessel coronary artery bypass graft was admitted for

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Figure 1. Left: Preservation of gray-white matter differentiation. Right: Hemorrhage of the left inferior cerebellum.

evaluation for orthotopic heart transplant. He had been progressively decompensating over the past 5 months with severely diminished exercise tolerance and cardiac cachexia. Two months prior to this admission, he underwent plain balloon angioplasty and stent placement for occluded vein grafts. His left ventricular ejection fraction from the month prior to admission was 19%.

Three weeks into his hospital course, while awaiting a donor heart, the patient became unresponsive in pulseless ventricular tachycardia. He received immediate chest compressions and was shocked once. Return of spontaneous circulation was achieved in 3 minutes, and he did not receive therapeutic hypothermia (TH) due to rapid recovery to baseline neurological status.

Three days later, the patient underwent orthotopic heart transplant. The operation was approximately 11 hours in duration and technically difficult due to dense adhesions and extensive coagulopathy. He also required replacement of the ascending aorta and hemiarch under hypothermic circulatory arrest and retrograde cerebral perfusion. One hour postoperatively, he became hypotensive leading to cardiac arrest with pulseless electrical activity. Immediate chest compressions were performed for 10 minutes, the chest was opened at the bedside, and direct cardiac massage was applied. The patient was cannulated, and venoarterial extracorporeal membrane oxygenation was initiated within 30 minutes. The patient received a heparin infusion as part of the anticoagulation protocol to prevent thrombotic complications. Therapeutic hypothermia was contraindicated due to significant underlying coagulopathy requiring multiple blood and factor transfusions. Treatment was empirically initiated for hyperacute rejection with high-dose intravenous corticosteroids, plasmapheresis, and antithymocyte globulin.

Initial neurological examination performed off sedative medications was significant for miotic pupils and partially intact oculocephalic reflexes. Within 1 day, he remained comatose and was noted to have spontaneous and stimulus-induced facial, eyelid, and limb movements consistent with generalized, multifocal myoclonus that persisted for 24 hours. Electroencephalogram showed no epileptiform discharges and reactivity was present. Antiepileptic therapy was not initiated. Neuron-specific enolase obtained 52 hours following cardiac arrest was 68 ng/mL.

The patient remained on ECMO for a total of 7 days after cardiac arrest. Neurological examination performed 4 days after the second episode of cardiac arrest was markedly improved with spontaneous eye-opening and tracking. Over the following week, the patient was following commands and withdrawing to pain symmetrically in all extremities. Neuroimaging performed 2 weeks postoperatively revealed normal gray-white matter differentiation and an incidental left inferior cerebellar hemorrhage that may have been related to anticoagulant therapy (Figure 1). After 3 weeks, the patient was verbally communicating, disoriented but attentive, with a mild left-sided hemiparesis. During the fourth week after cardiac arrest, he was ambulating with moderate assistance.

Discussion

Current practice guidelines state that serum NSE concentrations greater than 33 ng/mL at days 1 to 3 post-cardiopulmonary resuscitation (CPR) or status myoclonus within 1 day may be used to prognosticate poor neurological outcomes in patients following cardiac arrest.¹ To our knowledge, this is the first reported case of a patient who had an excellent neurological recovery, despite the concurrent presence of both of these traditional markers of poor prognosis.

There is biological plausibility for higher baseline NSE concentrations in patients who receive ECMO. Due to circuit shear stress, mechanical circulatory devices may induce hemolysis of red blood cells, which endogenously contain NSE.^{3,6} A recent case series reported that 3 of 31 patients who received ECMO recovered with good neurological outcome, despite NSE concentrations that exceeded 33 ng/mL. However, these patients also received TH, which may independently alter the kinetics of serum NSE release and decrease the positive predictive value at the 33 ng/mL threshold.^{3,7} Current practice guidelines do not differentiate between patients who receive mechanical circulatory support or TH and the potential alteration in baseline NSE concentrations. Furthermore, these guidelines do not provide specific recommendations, such as trending serial measurements, which may improve the predictive value^{8,9} and do not account for variability in laboratory testing techniques.^{10,11}

As with NSE, the positive predictive value of status myoclonus for detecting poor prognosis may be diminished in patients with cardiac arrest who receive TH. In a recent observational registry-based study of cardiac arrest, patients who received TH and demonstrated status myoclonus, 9% recovered with good neurological outcome.¹² The effect of ECMO on the prognostic value of status myoclonus has not been systematically studied, although myoclonus has been reported as an independent neurological finding in association with ECMO.¹³

There were possible confounders in this case that may have contributed to elevated NSE levels that warrant discussion. The patient had a brief cardiac arrest episode with rapid recovery to baseline neurological status 1 day prior to the second cardiac arrest episode. This first cardiac arrest episode may have contributed to some modest degree of NSE elevation that was perhaps sustained in the context of hypothermia during orthotopic heart transplant that occurred 3 days later. We found no reliable report in the literature that antithymocyte globulin, plasmapheresis, or intravenous steroids could increase NSE levels. The cerebellar hemorrhage discovered on brain computed tomography was incidental and may have been related to anticoagulant therapy used during ECMO. Intracerebral hemorrhage may contribute to moderate elevations in NSE.¹⁴ These clinical variables further emphasize the need to interpret prognostic factors carefully in the context of each individual case.

In summary, reliable prognostic markers could significantly improve the quality of end-of-life decision-making after cardiac arrest. Existing practice guidelines do not reflect recent advances in cardiopulmonary and neurological therapeutics such as ECMO and TH. This case report underscores the need for a conservative and multimodal approach to neurological prognostication following cardiac arrest that interprets prognostic factors in the context of each individual case. Future studies are indicated to establish reliable prognostic markers and/or thresholds in patients treated with ECMO or other mechanical circulatory interventions.

Declaration of Conflicting Interests

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