

CASE CONFERENCE

AGITATED DELIRIUM AND SUDDEN DEATH: TWO CASE REPORTS

Kenneth S. Park, MS, Carrie S. Korn, RN, Sean O. Henderson, MD

Agitated delirium (AD), sometimes referred to as excited delirium, is characterized by an acute onset of bizarre and violent behavior and may be accompanied by combativeness, hyperactivity, unexpected "super-human" strength, paranoid delusions, incoherent shouting, hallucinations, and hyperthermia.^{1,2} Underlying causes of AD include manic-depressive psychosis, chronic schizophrenia, intoxication with sympathomimetics or anticholinergics, cocaine intoxication, alcohol withdrawal, and head trauma. Since emergency medical services (EMS) or police are frequently the first to encounter these patients, many times without adequate event or medical history, caution is warranted in the restraining techniques utilized. These patients may, after being restrained either physically (e.g., being tackled and/or placed in physical restraints) or chemically (e.g., with haloperidol), suddenly go into respiratory or cardiac arrest.^{1,3-7}

We describe two cases of AD that highlight the predominant theories on this subject. In both cases, the patients were under the supervision of medical personnel when they became unresponsive.

CASE 1

A 45-year-old African American man with a history of schizophrenia was found standing at the corner of a motel office, shaking his head violently, hallucinating, and resisting aid. Police and EMS were summoned and, after an initial struggle, the patient was manually restrained and strapped to the gurney in a supine position. Paramedics

were unable to obtain vital signs due to the combative nature of the patient, but noted no overt signs of trauma. The skin was warm and dry, and the pupils were midrange and reactive. Although the patient entered the ambulance awake and alert, he became markedly less responsive during transport, with a rapid decrease in mental status. Within 15 minutes he progressed to cardiopulmonary arrest with an asystolic rhythm.

The paramedics intubated him with a Combitube and began advanced cardiac life support interventions. Despite drug therapy with epinephrine, atropine, and dextrose, the patient remained in asystole.

The patient arrived in the emergency department (ED) in asystolic cardiac arrest. His pupils were now fixed, midrange, and nonreactive. Although proper placement of the Combitube was confirmed, it was replaced with an endotracheal tube as per ED protocol. Central venous access was obtained, and standard resuscitative measures were continued. The patient remained in asystole and was pronounced dead 22 minutes after arrival.

CASE 2

A 41-year-old African American woman with a history of polysubstance abuse was brought to the ED by police and paramedics for bizarre behavior including slamming her head against a brick wall. On arrival, she was combative, speaking in incoherent sentences, and refusing to stay on a gurney. Minutes after her arrival she was administered haloperidol 5 mg IM and hospital police arrived to restrain her. The safety personnel placed her in a sitting position on the gurney with her wrists handcuffed to her ankles. The patient suddenly collapsed with no spontaneous respirations or pulse. Cardiopulmonary resuscitation was initiated. Electrocardiographic monitoring revealed pulseless electrical activity, and the patient was intubated and immediately given epinephrine 10 mg via the endotracheal tube. Intravenous access was obtained and the patient was given atropine 1 mg and naloxone 2 mg IV. Within 7 minutes a pulse returned at a rate of 172 beats/min, with a blood pres-

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Address correspondence and reprint requests to: Carrie S. Korn, RN, Department of Emergency Medicine, LAC+USC Medical Center, 1200 North State Street, Room 1011, Los Angeles, CA 90033. e-mail: <ckorn@hsc.usc.edu>.

sure of 222/113 mm Hg. The patient had a rectal temperature of 40.6°C (105°F).

Blood chemistries were within normal limits except for an elevated BUN and creatinine. Other laboratory results were significantly abnormal: pH 6.93, a white blood cell count of 18,500/ μ L blood, a hemoglobin of 11 gm%, a hematocrit of 34.4%, and a bicarbonate of 11 mM. Urine analysis showed large hemoglobin and the urine toxicology screen was positive for cocaine and opiates.

Computed tomography (CT) of the patient's head showed signs of anoxic encephalopathy. Electroencephalography (EEG) showed slow diffuse encephalopathy. The patient remained acidotic and was treated for rhabdomyolysis while in the intensive care unit. Her brainstem reflexes continued to deteriorate. Nine days after admission, EEG showed no brainstem function. The patient was extubated and died.

DISCUSSION

The incidence of AD is unclear due to the lack of good prospective studies and the bias of retrospective studies to select cases of fatal AD. Case reports have clustered in summer months and in areas noted for high temperature and high humidity.⁸ A body mass index (BMI: weight [kg]/height [meter²]) in the upper three quartiles may increase risk for fatal AD.⁹ It is uncertain whether AD always leads to cardiopulmonary arrest or whether the literature has simply focused on cases of fatal AD because they were memorable, and has thus missed reporting cases of AD that were successfully treated.

There are several predominant theories on the cause of sudden death in patients with AD: positional asphyxia, metabolic acidosis, rhabdomyolysis, and catecholamine-induced sudden death. Positional asphyxia has been suggested due to the common occurrence of patients' dying shortly after they were placed in physical restraints in a prone position, particularly after being "hog-tied."^{4,6,7} This consists of placing the subject prone and binding wrists and ankles together behind the back.^{4,6,10} Studies of the effects of hog-tying on respiratory function in *healthy* subjects have been inconclusive^{10,11}; however, the U.S. Department of Justice has issued a guidance statement cautioning against the use of hog-tying.¹²

O'Halloran and Lewman suggest that three factors contribute to increasing oxygen demands and decreasing oxygen delivery in patients with AD resulting in death: 1) the state of AD combined with police or EMS confrontation places catecholamine stress on the heart; 2) hyperactivity with struggling against both police and restraints increases oxygen delivery demands on the heart and lungs; and 3) breathing is hindered by being hog-tied, making it difficult to expand the chest wall and depress the diaphragm.⁴

Metabolic acidosis was addressed in a recent case series by Hick et al., who stated that metabolic acidosis can be associated with cardiovascular failure following exertion in a restrained position.¹³ The increased levels of exercised-induced lactic acid and the alteration in pain sensation from psychosis and delirium results in severe acidosis with maximal sympathetic discharge. Early intervention by EMS personnel with benzodiazepine sedation may increase the survival rate of AD patients, though this has not been studied.

Ruttenber et al. suggest that AD and cocaine-associated rhabdomyolysis (CAR) are part of a syndrome found in chronic cocaine users.⁸ Rhabdomyolysis has been noted in a number of patients with cocaine-induced AD.^{8,9} It is associated with hyperthermia, agitation, hyperactivity, and bizarre behavior. Patients surviving the initial cardiac arrhythmias may develop CAR, particularly if they have hyperthermia.^{8,14}

The role of catecholamines and stress has been studied in cases of sudden death. It is widely accepted that stress may increase the mortality of preexisting heart conditions.^{5,15} Mets et al. suggest that catecholamines pharmacokinetically enhance the toxicity of cocaine leading to seizures, respiratory arrest, and cardiac arrest in rats.¹⁶ It is thought that patients with AD may be sensitive to catecholamines due to their history of cocaine use or schizophrenia.^{5,16,17} Neuronal catecholamine release may cause arrhythmias,¹⁵ and in a patient with AD, the additional stress of confrontation with law enforcement officials or medical personnel may lead to cardiopulmonary arrest.⁵

The two cases presented here are examples of these current theories on sudden death in AD. Although the definite cause of death in case 1 is uncertain, the case history is consistent with catecholamine-induced sudden death. The patient was not restrained in a prone position and was not hog-tied. He had no signs of rhabdomyolysis, and although his temperature was not taken, paramedics noted that his skin was not hot and appeared normal. Although there is no way to prove that the patient's death was stress-induced, we know that he was agitated and that he struggled with paramedics. Presumably, he was under emotional stress, and his sudden quiescence combined with his prior behavior is consistent with catecholamine-induced sudden death.

Case 2 is a complicated case that does not suggest an obvious single etiology leading to cardiac arrest. Safety personnel had placed the patient in a sitting position with her wrists handcuffed to her ankles, so that she was bent forward, placing pressure on her chest, a risk factor for positional asphyxia. In addition, she showed evidence of rhabdomyolysis, and was hyperthermic and acidotic. All of these conditions may have contributed to her going into cardiopulmonary arrest.

The approach to a patient with AD is a delicate matter. The patient is frequently destructive, and all precautions must be taken to ensure the safety of the patient and EMS personnel alike. At the same time, if the patient is handled too roughly, or if the patient continues to struggle against restraints, he or she may go into a profound metabolic acidosis or a catecholamine-induced sudden death. Even the mere presence of law enforcement officials may overly agitate a patient. Patients in an AD state should be approached cautiously and calmly. The patient should not be restrained in a prone position if at all possible. Maintaining the patient in a supine or lateral position may help minimize the risk of a compromised airway. In an effort to prevent continued combativeness while the patient is restrained, which can lead to possible metabolic acidosis, EMS personnel should consider benzodiazepines for sedation. Rhabdomyolysis may be treated with intravenous fluids, and active cooling measures should be implemented against hyperthermia.

Patients with AD, especially those who have a history of cocaine use or psychosis, are at risk for sudden death. Personnel should be especially aware of any fluctuation in the patient's activity level. Respiratory and cardiac function should be monitored. Emergency medical personnel should be aware of the possible complications of AD and be prepared to address them.

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