Tales from the MH Hotline

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From the many calls received at #800-644-9737, the MH Hotline supported by MHAUS, we have selected three from the third millennium to present to you today. These three patients each had life-threatening complications of inhalation anesthesia, indeed one of them died. The management of the cases differed somewhat and the diagnostic pathway that produced a pathologic diagnosis also differed. The differences between these cases illustrate why it is important to pursue the definitive diagnosis after treatment of the crisis.

Case #1, in 2004:

A 4-yr-old, ASA 1, boy from Mexico presented for ASD closure.

There were no known relevant familial diseases or problems with general anesthesia. Induction of anesthesia was accomplished with sevoflurane,and maintenance with isoflurane, fentanyl, and pancuronium. On arrival to the cardiac intensive care unit, residual neuromuscular blockade was antagonized with atropine and neostigmine, and the trachea extubated when the patient was awake and strong.

Twenty minutes later, the patient developed a wide-complex bradycardia which progressed to ventricular fibrillation. Serum potassium was > 9 mEq/L. Resuscitative measures were successful following administration of calcium, glucose-insulin, and bicarbonate. Serum creatine kinase (CK) within an hour of the arrest was 17,821 U/L, and peaked at 613,120 U/L 48 hrs postoperatively. The urine was noted to be pale pink in color.

The MH Hotline was then consulted with the following questions:

Could this clinical episode represent MH?
Is dantrolene indicated at this time?
Could this be a manifestation of an occult myopathy?
If so, how would I confirm the diagnosis?

Case # 2, in 2002:

A 5 yr-old, 28 kg, boy presented for repair of nondisplaced jaw fracture. Past medical and surgical history were unremarkable. He had undergone bilateral herniorraphy without complications. Others in his family had anesthesia without problems. He co-operated with gradual induction of anesthesia by inhalation of nitrous oxide and halothane. After placement of an intravenous catheter, direct laryngoscopy and uncomplicated tracheal intubation,
isoflurane replaced halothane and surgery began. Twenty-five minutes after induction of anesthesia, end-tidal CO_2 was greater than 60 mmHg with spontaneous respiratory rate greater than 40/min. Heart rate had increased from 80/min to 120/min. Manually controlled ventilation could not reduce the end-tidal CO_2 below 60 mmHg. Compliance of the respiratory system was normal. The jaw and the arms were not stiff, but the legs were so stiff that the knees and ankles could not be bent. Skin temperature was 33.7 C. Five minutes later isoflurane was stopped, propofol was given, skin temperature was 37.8 C. Rigidity and hypercarbia continued while ventilation remained easy. Five minutes later another IV catheter was placed and ice packs were placed around the child while the oxygen was switched to a ‘clean’ source. Five minutes later 100 mg dantrolene was administered. Within two minutes end-tidal CO_2 and temperature decreased.

Is this enough dantrolene?

Prior to transport from surgery center to pediatric intensive care by ambulance 20 mg more dantrolene was given. Arterial blood gases were normal. K^+ was 5.1 mEq/L. CK was 14,000 U/L. The diagnosis is presumed malignant hyperthermia.

How can this be confirmed?

Case #3, in 2003:

A 10 yr-old, 44 kg, ASA I boy presented for bilateral repair of congenital ptosis. Review of systems was negative. The father had surgery for ptosis repair as a child without problems. There was no family history of problems with anesthesia, heat intolerance or myopathy. Physical exam was unremarkable except for bilateral ptosis.

Anesthesia was induced with sevoflurane (max 8%) and N_2O without difficulty. An endotracheal tube was easily placed without the use of muscle relaxants. Anesthesia was maintained with sevoflurane 2.5% and N_2O with spontaneous ventilation. The first hour of the anesthetic proceeded with blood pressure of 120/60 to 140/70 mmHg, a sustained heart rate of 155/min after glycopyrrolate 5 mcg/kg, spontaneous respiratory rate of 20 to 24/min, end-tidal CO_2 52 to 60 mmHg, pulse oximetry saturation of 100% and axillary skin temperature of 36 C. In the following hour there were occasional premature ventricular conductions and a drop in oxygen saturation to 91% when FiO_2 was 50%. The surgeon simultaneously noted that the child felt warm and end-tidal CO_2 increased to 75 mmHg despite controlled ventilation.

Sevoflurane was discontinued and propofol given. Treatment for MH was begun. As an arterial catheter was placed, the arm which had been flaccid became rigid. As the first dose of dantrolene was being administered, 5 minutes after the onset of abnormal clinical signs, asystole occurred. CPR was immediately initiated including multiple doses of atropine, epinephrine, HCO_3, glucose, insulin, lidocaine and dantrolene (10 mg/kg). Maximum temperature during CPR was 40.8 C.

In the ICU the child was treated for pulmonary edema, disseminated intravascular coagulation, and myoglobinuria. Dantrolene was continued at 1 to 2 mg/kg Q 6 hours. Despite improvement in blood gases and cardiovascular status, he remained neurologically unresponsive with fixed pupils. Eight hours later the base deficit increased to –5, temperature increased to 39 C, while minute ventilation, pCO_2 stayed the same and heart rate continued at 130/min.

Why is the temperature up? Is this a recrudescence of MH? What other causes could there be? What treatment should be given?

The child has pinpoint pupils and is unresponsive to painful stimuli and flaccid. **What could be the explanation for this neurologic status? Can any treatment be provided?**

The orthopedic surgeon evaluated the child and feels that the child has compartment syndromes in his calves. A fasciotomy is performed at the bedside.
That evening the child suddenly becomes bradycardic, hypertensive and is unresponsive to resuscitation.

What tests would you request to obtain a pathologic diagnosis?

References:

Bouchama A, Knochel JP. Heat stroke. New Eng J Med 2002; 346:1978.

Breucking E, Reimnitz P, Schara U, Mortier W. Severe anaesthetic incidents in patients and families with Duchenne and Becker type muscular dystrophy. Anaesthetist 2000; 49:187.

Flewellen EH, Nelson TE, Jones WP, and others: Dantrolene dose response in awake man: implications for management of malignant hyperthermia. Anesthesiology 1983; 59:275.

Girard T, Treves S, Voronkov E, Siegemund M, Urwyler A. Molecular genetic testing for malignant hyperthermia susceptibility. Anesthesiology 2004;100:1076.

Ibarra CA, Murayama K, Wu S, Ichihara Y, Kikuchi H, Ochiai R, et al. Malignant hyperthermia in Japan: Genetic screening of the entire coding region in the type 1 ryanodine receptor gene. abstract A718 American Society of Anesthesiologists 2005 Annual Meeting.

Larach MG, Localio AR, Allen GC, and others: A clinical grading scale to predict malignant hyperthermia susceptibility. Anesthesiology 1994; 80:771.

Larach MG, Rosenberg H, Gronert GA, Allen GC. Hyperkalemic cardiac arrest during anesthesia in infants and children with occult myopathies. Clin Pediatr (Phila)1997; 36:9.

Larach MG, Rosenberg H, Gronert GA, Allen GC. Did anesthetics trigger cardiac arrests in patients with occult myopathy? Anesthesiology 2001; 94: 933.

Lerman J, McLeod ME, and Strong HA: Pharmacokinetics of intravenous dantrolene in children. Anesthesiology 1989; 70:625.

Levano S, Singer M, Urwyler A, Girard T. Screening for novel mutations in the coding region of the ryanodine receptor in individuals with malignant hyperthermia susceptibility. [abstract] In: XXIVth Annual Meeting of the European Malignant Hyperthermia Group. Mainz, Germany 2005, p. 59.

Sambuughin N, Holley H, Muldoon S, Brandom BW, de Bantel AM, Tobin JR, et al. Screening of the entire ryanodine receptor type 1 coding region for sequence variants associated with malignant hyperthermia susceptibility in the North American population. Anesthesiology 2005;102:515.

Sei Y, Sambuughin NN, Davis EJ, Sachs D, Cuenca PB, Brandom BW, et al. Malignant hyperthermia in North America: genetic screening of the three hot spots in the type I ryanodine receptor gene. Anesthesiology 2004;101:824.

See www.emhg.org for the criteria that a sequence variant must meet to be considered causative of MH and the list of *RYR1* sequence variants that have met those criteria.