A Case Report of Malignant Hyperthermia in a Dental Clinic Operating Room

M. Cynthia Fukami, DMD, MS,* and Steven I. Ganzberg, DMD, MS*†

*Department of Dentistry, Columbus Children's Hospital, Columbus, Ohio, and †Department of Oral and Maxillofacial Surgery, The Ohio State University College of Dentistry, Columbus, Ohio

A healthy 5-year-old boy presented for arch bar placement under general anesthesia in an operating room in a dental school. The patient had previously undergone general anesthesia without complication, and no family history of anesthetic problems were reported. Halothane mask induction, intravenous catheter placement, and nasal intubation proceeded uneventfully without the aid of a muscle relaxant. Halfway through the procedure, signs and symptoms of malignant hyperthermia, including muscle rigidity, hypercarbia, tachypnea, and tachycardia were noted. Immediate treatment, including discontinuation of the triggering agent, dantrolene administration, and cooling measures were applied, and once stable, the child was transferred to Columbus Children's Hospital for further management. The patient experienced no postoperative complications. Further discussion regarding the pathophysiology and management of malignant hyperthermia is provided.

Key Words: General anesthesia; Malignant hyperthermia; Dantrolene.

Malignant hyperthermia (MH) is an entity that is widely feared and yet rarely encountered. In hospitals with multiple operating rooms where potent inhalation agents and succinylcholine are commonly used, the occurrence of an MH episode is anticipated. We describe a case of an acute onset of an MH episode in the less likely setting of a dental clinic in which a child underwent intubated general anesthesia for an oral surgical procedure. This case report describes the identification and management of this life-threatening condition. The proposed mechanism and treatment of MH is further discussed.

CASE REPORT

A 5-year-old boy was scheduled for closed reduction with intermaxillary fixation to address a left condylar and right parasymphyseal mandibular fracture sustained after he fell from a horse and was kicked in the face. The

child had a history of asthma treated with cromolyn sodium and inhaled albuterol. The patient had previously undergone general anesthesia for bilateral ear tube insertion without complication. No family history of problems with anesthesia was elicited as neither the parents nor siblings had undergone any surgical procedures.

The patient was brought to an operating suite in the College of Dentistry, having been NPO for solids for over eight hours, with unrestricted water until 3 hours prior to induction. The patient received 2 puffs of albuterol by inhaler preoperatively for asthma prophylaxis. The child was cooperative, and monitors including noninvasive blood pressure (NIBP) cuff, pulse oximeter (SpO₂), electrocardiogram leads and an axillary skin temperature probe were placed. Slow mask induction with increasing increments of halothane in nitrous oxide and oxygen proceeded without incident, with easy mask ventilation. Following onset of general anesthesia, a 22 g catheter-over-needle was placed in the dorsum of the right hand, and a slow infusion of D5LR was started. Twenty milligrams of lidocaine IV was administered, nitrous oxide was discontinued and 100% oxygen with halothane was continued. After an appropriate depth of anesthesia was obtained, the patient was intubated without difficulty via the right nares with a 5.5 nasal RAE

Received June 14, 2004; accepted for publication September 29, 2004.

Address correspondence to Dr M. Cynthia Fukami, Department of Dentistry, Columbus Children's Hospital, 770 Children's Drive, Columbus, OH 43205; fukamic@chi.osu.edu.

Anesth Prog 52:24-28 2005
© 2005 by the American Dental Society of Anesthesiology

ISSN 0003-3006/05/\$9.50
SSDI 0003-3006(05)

tube. No neuromuscular blocking agent was given. Bilateral breath sounds without wheezing and equal chest rise were noted, and end-tidal CO_2 (EtCO_2) was detected by capnography. The tube was secured, the eyes were taped, the head was wrapped, and a blanket was placed. After intubation, anesthesia was maintained with isoflurane with 66% nitrous oxide in oxygen. The patient continued spontaneously ventilating without difficulty. The surgeons injected 7.2 mL of 2% lidocaine with 1:100,000 epinephrine intraorally and proceeded with arch bar placement.

Baseline measurements at onset of surgery were SpO_2 at 99%, NIBP at 100/40, heartrate (HR) at 90 beats per minute (BPM), EtCO_2 at 44 mmHg, and skin temperature at 33.5°C. Approximately 25 minutes after induction, the following changes from baseline were noted: the EtCO_2 had risen to 60 mmHg, the spontaneous respiratory rate was above 40 bpm, and the heart rate had risen to 120. The skin temperature was still 33.7°C. NIBP also was unchanged. We began manually hyperventilating the patient without difficulty, but the EtCO_2 remained above 60 mmHg. Bilateral breath sounds without wheezing were maintained. Upon patient survey, no masseter rigidity was detected, and the upper extremities remained supple. However, the lower extremities were extremely rigid, and the patient's knees and ankles would not bend upon manipulation. At that point, the EtCO_2 had risen into mmHg range in the 70s, and the HR was now in the 140s. Isoflurane was discontinued and 100% O_2 was given. We continued manual hyperventilation and maintained anesthesia with continuous boluses of propofol. The lower extremities remained rigid and warm to touch, and when the patient was allowed to spontaneously ventilate, the EtCO_2 quickly rose to over 80 mmHg. The SpO_2 had also decreased gradually to its lowest point of 95%. At this point the skin temperature was only 34–35°C.

A presumptive diagnosis of malignant hyperthermia was made, and the emergency cart containing a malignant hyperthermia kit was obtained. EMS was activated and the clinic nurse apprised Columbus Children's Hospital (CCH) of the situation. A second 20 g IV was obtained at the left hand, and 0.9 normal saline was administered through both IV lines. Dantrolene was reconstituted with sterile water as quickly as possible and given through both lines; a total of 100 mg dantrolene was given over the next 15 minutes. The axillary skin temperature at this point had risen to 37.8°C at maximum but within the first 1–2 minutes following the initial dose of dantrolene, a rapid decrease in the skin temperature to 36.5°C and a drop in EtCO_2 by approximately 10 mmHg was noted. Concurrently, the circle-type breathing circuit had been replaced with a Bain circuit, and switched to a portable oxygen/nitrous oxide

unit. Manual hyperventilation with 100% oxygen was continued without difficulty, and breath sounds were frequently evaluated. The blanket and headwrap had been removed, and ice packs were placed in the axillary and groin areas of the patient for cooling. Propofol was discontinued and 3 mg midazolam IV was given for amnesia. The IV fluids were switched to ice-cold 0.9NS. A 12 French nasogastric tube was placed in the left nares for iced gastric lavage and suction. Five milligrams of furosemide IV was administered immediately prior to transport. There was no electrocardiographic evidence of hyperkalemia.

While therapeutic and supportive measures were being administered, the oral surgeons quickly completed arch bar placement, but did not place intermaxillary fixation wires, which could be accomplished at a later date without general anesthesia. The patient's vital signs continued to improve; the vital signs immediately prior to transport were: SpO_2 at 99%, NIBP at 92/37, HR at 99 bpm, and EtCO_2 at mmHg range in the 40s with manual ventilation.

The EMS squad arrived 15 minutes after the initial dose of dantrolene, and the parents were informed and were allowed to see their son. The intubated patient was transported with continuous monitoring via ambulance to CCH, escorted by the dentist anesthesiologist, dental anesthesia resident, and attending oral surgeon. The patient received an additional 20 mg of dantrolene during transport. Vital signs were stable, and manual ventilation was continued without difficulty.

Upon arrival at CCH's Emergency Department, vital signs were stable: SpO_2 was 100%, HR was 90 bpm, and NIBP was 109/59. Rectal temperature was recorded at 98.2°F. No muscle rigidity was noted. A total of 2 liters of fluid had been given throughout the course of treatment and a Foley catheter was placed immediately, which drained 400 cc of clear, light yellow urine over the next 45 minutes. Shortly after arrival, the patient began "bucking" on the tube and was given 3 mg midazolam and 3 mg vecuronium IV, which allowed for easy manual ventilation. An arterial line was placed at the left wrist, and the initial arterial blood gas showed no metabolic acidosis (pH 7.44/ PaCO_2 32/ PaO_2 490/ HCO_3 23/BE -2.6), high normal potassium at 5.1 mEq/L, and reduced ionized calcium at 1.07 mmol/L. A chest X-ray confirmed endotracheal tube placement, and showed mild fluffy perihilar infiltrates bilaterally.

The parents were informed of the patient's condition and progress, and he was admitted to the intensive care unit. He was extubated later that evening without complication, and kept in the intensive care unit overnight. Creatine kinase levels were elevated (CK 1429 U/L) upon admission, and continued to be elevated the following morning (CK 4080 U/L). However, no recru-

descent of signs and symptoms were observed, and the patient did not receive additional medication. During a follow-up visit by the attending dentist anesthesiologist the following morning, he was awake, eating, and interactive. He was discharged by the pediatric medicine team on that day to home with no need for further medication or medical follow-up. Per report, his recovery at home was uneventful.

The patient was seen 6 weeks later at CCH's operating room for removal of the arch bars. He underwent nontriggering general anesthesia without consequence. After the surgery, he was kept in isolation in the recovery area so that his exposure to inhalation agents from the other recovering children was minimized. Creatine kinase levels remained normal during this surgery.

His parents subsequently contacted the Malignant Hyperthermia Association of the United States (MHAUS). The MHAUS consultants delayed the muscle biopsy until 6 months following the suspected MH episode, to ensure complete healing and recovery to baseline before obtaining a muscle sample. Per report from his parents, the child tested positive for MH with the muscle biopsy. Other related family members are scheduled to be tested. Of interest, his mother informed us in a follow-up conversation that her aunt reportedly had "stiffness following surgery" in the 1960s, which the parents were unaware of at the time of the surgery.

DISCUSSION

The pathophysiology of MH is still not fully understood. During an acute episode of malignant hyperthermia, intracellular calcium increases in skeletal muscle, causing uncontrolled muscle contractions. It appears that there may be a defect in the RYR1 gene for the ryanodine receptor, a calcium channel receptor in the sarcoplasmic reticulum.^{1,2} The abnormal receptor releases excess calcium once triggered by specific agents, mainly succinylcholine and/or the halogenated inhalation agents. This theory has not been consistently upheld, as it does not explain why MH does not strike during every episode of general anesthesia in MH-susceptible patients,³ nor why some patients without the genetic defect still can develop MH. Indeed, this patient had previously undergone a brief general anesthetic without incident, and developed an MH crisis during this case even though succinylcholine had not been given.

The abnormal muscle contractions explain the multiple signs observed during an MH crisis.^{1,2} Muscle rigidity, particularly masseter spasm, may be noted initially. Increased muscle contractions lead to a hypermetabolic state, resulting in increased CO₂ production and metabolic acidosis, as well as increased core temperature.

The earliest signs of MH include unexplained tachycardia, particularly in association with increasing EtCO₂, and compensatory tachypnea in the spontaneously breathing patient or overbreathing of the ventilator if mechanically ventilated. A mild drop in pulse oximetry values is also consistent with the increased metabolic oxygen requirement. Hyperthermia is a relatively late sign. The overactive muscle cells lyse, releasing intracellular potassium; the resultant hyperkalemia can lead to dangerous cardiac bradydysrhythmias. The massive release of cellular contents in addition to the increasing metabolic acidosis may create generalized electrolyte disturbances, as well as myoglobinemia, which can lead to serious renal complications.

Successful management of the acute MH episode involves early diagnosis with immediate and early administration of dantrolene.¹ The mortality rate from MH was reduced from 80% to 10% following the development of dantrolene.³ Dantrolene binds to the ryanodine receptors and blocks calcium release, thereby halting the uncontrolled muscle contractions. Dantrolene is stored in 20 mg lyophilized aliquots with 3 gms of mannitol and must be reconstituted with 60 cc sterile water per vial. Dantrolene cannot be mixed with normal saline or Lactated Ringer's as it precipitates in these solutions. The recommended dose is 2–3 mg/kg every 5 minutes, up to a total dose of 10 mg/kg if needed. Reconstituting dantrolene is time-consuming and cumbersome, and calling for help immediately is crucial. This patient underwent a clear and rapid improvement with the initial dose of dantrolene, but additional doses may be required before an effect is seen. For a larger adult patient, this may involve mixing many bottles of dantrolene, and it may take several minutes for a single person to administer a larger bolus of the drug.

In addition to dantrolene, other immediate interventions include discontinuation of the triggering agents. Changing the breathing circuits and switching to an agent-free oxygen source is recommended, although high fresh oxygen flow will flush the circuit quickly. In this case, the portable O₂/N₂O unit typically used in dental offices was readily available, and was used to reduce continued exposure of the patient to either isoflurane or halothane which might have still been present in the CO₂ absorber, breathing circuit or anesthesia machine. Hyperventilation with 100% O₂ will help remove the triggering agent and accumulated CO₂ as well as compensate for the increased metabolic oxygen requirement. Cooling techniques such as gastric lavage or placing ice internally and externally can help lower core temperature. Using ice-cold IV fluids will also rapidly decrease core temperature. Serial blood gas can be taken to evaluate metabolic acidosis, electrolyte imbalances, and markers of muscle metabolism. This is difficult to obtain

in an outpatient setting, and we were unable to evaluate specific electrolyte abnormalities until this child was brought to the CCH emergency department. To treat hyperkalemia, insulin and dextrose, along with furosemide, can be used. Although no EKG changes consistent with hyperkalemia were noted, furosemide was given empirically to treat potential hyperkalemia, while inducing diuresis to help prevent renal failure secondary to myoglobinuria. Metabolic acidosis should be treated with sodium bicarbonate and continued hyperventilation.

Managing a MH crisis requires multiple interventions which must occur quickly, and having additional help is critical. Several anesthesia-trained personnel were present in this case, which is less common in a private practice setting. In addition to a staff dentist anesthesiologist, there were 2 dental anesthesia residents and an oral surgery team who were cognizant of MH management. The clinic nurse was also instrumental in contacting the hospital team, as well as obtaining medications and equipment. Both early intervention and the presence of multiple trained personnel contributed to the successful outcome of this case, as evidenced by the absence of morbidity and minimal changes in laboratory values.

Following stabilization of the patient, he or she should be admitted for observation into an intensive care unit for at least 24 hours to monitor for complications from the initial episode, as well as possible reemergence of the MH crisis. Although this is readily accomplished when an MH crisis occurs in a hospital operating room, an outpatient must be transported to the emergency department of the local hospital, preferably a pediatric hospital if a child is involved. Dantrolene has a half-life of 6 hours, and may need to be given intravenously again should MH signs reappear. Because dantrolene is a mild muscle relaxant, it should be given to a monitored patient, with oxygen and ventilatory support immediately available. Stabilized patients may continue to receive several doses of oral dantrolene as well. Serial blood gases should be obtained to monitor acidosis and enzyme markers such as creatine kinase, which may indicate continued muscle breakdown. Acute renal failure secondary to myoglobinuria is the most common morbidity and must be evaluated.

While genetic testing is under development, a muscle biopsy test is the final confirmation of malignant hyperthermia susceptibility.^{1,4} A patient with a presumed MH episode may undergo this procedure at specific centers in the United States, in which a 1–2 cm incision is made in the thigh and muscle biopsy is taken. A highly-sensitive halothane-caffeine-contraction test is performed on the sample. In response to equal electrical stimulation, MH-susceptible tissue will contract significantly more than normal tissue when bathed in the different substrates. Since MH is autosomally dominant with var-

iable penetrance, testing is also recommended for related family members of patients with a positive contraction test.

For this patient and MH-positive family members, nontriggering anesthesia should be employed for all future surgeries. Patients with disorders associated with an increased incidence of MH, such as muscular dystrophy, should also undergo nontriggering anesthesia.¹ All halogenated inhalation agents and succinylcholine should be avoided. Where applicable, regional and local techniques utilizing local anesthetics are a safe option. Nitrous oxide is the only trigger-free inhalation agent, while barbiturates, propofol, etomidate, benzodiazepines, opioids, and nondepolarizing muscle relaxants are all safe to use. Ketamine is not a triggering agent, but its associated catecholamine release may mask the initial presentation of tachycardia during an acute MH event. For sedation and general anesthesia, with or without intubation, total intravenous anesthesia (TIVA) using nontriggering medications is an option.

If general anesthesia using an anesthesia machine is planned with a MH-susceptible patient, more precautions must be taken. The machine circuit should be cleared of past agent by actively flushing with 100% O₂ for at least 20 minutes prior to use, and a fresh breathing circuit should be attached. EtCO₂ and temperature, preferably core, should be continuously monitored. Dantrolene should be immediately available. For hospital operating rooms, the minimum recommended amount of dantrolene stored is 36 bottles, or 720 mg, which is roughly the equivalent of 10 mg/kg per adult patient. Cooling measures should be readily available, including an ice machine or packs, cold IV normal saline, and nasogastric tubes. Other medications which should be immediately available include lidocaine, insulin, dextrose, furosemide, and sodium bicarbonate.

Even without a positive history of MH, any practitioner using potent inhalation anesthetics or succinylcholine must be prepared to treat MH. Dantrolene and sterile water for injection (without bacteriostatic agent) must be readily available, but at current prices of \$60–70 per 20 mg bottle of dantrolene (Dantrium), this expense is more readily absorbed by a hospital or surgicenter than a dental office. For the dental office-based practitioner, one possibility is to carry enough dantrolene to cover the initial 2–3 mg/kg dose for an adult patient, particularly if hospital support is nearby.

Both patients and clinicians can access more information at the Web site for Malignant Hyperthermia Association of the United States (MHAUS), and emergency information can be obtained through their hotline.⁵ The Web site discusses the evaluation and management of MH patients, and provides a list of consultants and muscle biopsy test centers. The site also contains a rec-

ommended list of drugs and equipment to obtain in order to create an MH kit, which is especially necessary for anyone using triggering agents in their office.

REFERENCES

1. Rosenbaum HK, Miller JD. Malignant hyperthermia and myotonic disorders. *Anesthesiol Clin N Am*. 2002;20:385–426.
2. Hopkins PM. Malignant hyperthermia: advances in clinical management and diagnosis. *Br J Anesth*. 2000;85:118–28.
3. Strazis KP, Fox AW. Malignant hyperthermia: a review of published cases. *Anesth Analg*. 1993;77:297–304.
4. Rosenberg H, Antognini JF, Muldoon S. Testing for malignant hyperthermia. *Anesthesiology*. 2002;96:232–237.
5. Malignant Hyperthermia Association of the United States (MHAUS). Available at: <http://www.mhaus.org>. Accessed January 21, 2005.