Case Report

Successful Management of Hypothermic Cardiopulmonary Bypass in a Malignant Hyperthermia Susceptible Patient

Abstract

Malignant hyperthermia (MH) is a potentially lethal reaction in those that are genetically predisposed, frequently triggered by inhaled anesthetics. MH is often difficult to diagnose because it is accompanied by signs and symptoms that are shared with other disorders. The diagnosis is further obscured in cardiac surgical patients, as the signs of MH can be masked by the cardiopulmonary bypass circuit (CPB) and the use of induced hypothermia. In this case-report, we describe the successful anesthetic management of a 65-year-old MH-susceptible female, confirmed via caffeine halothane contracture test, with aortic regurgitation and ascending aortic dilatation who underwent a Bentall procedure. We have also identified certain key measures for the safe anesthetic management of these patients.

Keywords: *Cardiac surgery, cardiopulmonary bypass, inhaled anesthetics, malignant hyperthermia*

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Introduction

Malignant hyperthermia (MH) is a rare yet familiar lethal hypermetabolic disorder of skeletal muscle that can be triggered in susceptible patients on exposure to drugs used during anesthesia. While the nature of MH episodes during cardiac surgery may not differ substantially from those triggered during other operations, cardiac surgery does present unique challenges when caring for MH-susceptible patients. Herein, we present a patient with a prior history of MH who underwent an urgent cardiac surgery requiring hypothermic cardiopulmonary bypass (CPB).

Case Description

A 65-year-old Caucasian female with severe ascending aortic dilation and aortic regurgitation was scheduled for an urgent Bentall procedure. Her past medical history was remarkable for a recent laparoscopic cholecystectomy after which she developed MH in the immediate postoperative period. This required use of dantrolene and a prolonged ICU and hospital stay. Interestingly, her three prior general anesthetics for herniorraphy, hysterectomy, and orthopedic spine surgery had been uneventful. Family history revealed an aunt with a similar MH episode in the past. Because of the strong family history, immediate members of her family were advised to undergo the caffeine halothane contracture test. All tested positive.

Transesophageal echocardiography (TEE) was performed on the patient preoperatively. This was notable for a dilated ascending aorta measuring 61 mm at the level of the pulmonary artery, absence of aortic dissection and severe aortic regurgitation with a vena contracta of 7 mm and pressure half-time (PHT) of 165. During the TEE, the patient developed acute respiratory failure requiring emergent intubation facilitated by IV etomidate without use of muscle relaxant. There were no signs of MH following intubation. An urgent cardiac catheterization showed non-obstructive coronary artery disease (CAD) with a left ventricular end-diastolic pressure (LVEDP) of 22 mmHg.

The patient was urgently scheduled to undergo surgery. Since we do not have a dedicated anesthesia machine for MH- susceptible patients, we prepared our Drager Fabius anesthesia machine (Drager Medical, Telford, PA, USA) by removing all vaporizers, replacing CO_2 absorbent, attaching a fresh anesthesia circuit, and running 10 l fresh gas flow with tidal volume 1 l for 2 hours. We also

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removed succinylcholine from the drug tray, and kept dantrolene available in the room. The vaporizer from the CPB machine (Terumo System One®, Terumo CVS Corporation, Ann Arbor, MI, USA) was also removed.

A combination of propofol and sufentanil infusions was chosen for maintenance of anesthesia. Rocuronium was selected for skeletal muscle relaxation. Invasive blood pressure monitoring, central venous and pulmonary arterial pressure monitoring, and continuous cardiac output with mixed venous oxygen measurements supplemented the standard ASA monitors through the case. Intraoperatively, temperature was monitored using both nasopharyngeal probe and indwelling Foley catheter. Median sternotomy was followed by ascending aortic cannulation beyond the dilatation and a three-stage venous cannulation of the inferior vena cava through the right atrial appendage in preparation for the CPB. During CPB, ABGs were drawn every 20 min with special attention to $PaCO_2$ and base deficit. Heparin 300 Units/kg was administered and CPB was instituted after confirmation of activated clotting times of greater than 400 seconds. The patient was cooled to 33.1°C by the perfusionist to comply with surgeon's preference. Rewarming was uneventful, with strict maintenance of less than 1°C difference between nasopharyngeal and bladder temperatures. Following an uneventful CPB course, the patient was successfully weaned from CPB with infusions of epinephrine and vasopressin.

On postoperative day (POD) #3, she was successfully extubated. On POD #16, she was discharged from the hospital.

Discussion

MH is a potentially lethal complication of a rare inherited muscle disorder. Contact with triggering substances affects calcium homeostasis leading to massive calcium release from the sarcoplasmic reticulum in response to a defective ryanodine receptor.[1] This allows intracellular calcium levels to rise, producing sustained, uncoordinated muscle contractions, which in turn increase muscle work, O_2 consumption, CO_2 production, and lactic acid production.[2] As a result of these contractions, acidosis develops and temperature rises (body temperature may rise 1°C [1.8°F] or more every 5 min). Because of the life-threatening nature of MH, it is important to undertake special precautions for these patients. Cardiac surgery, and its use of extracorporeal circulation, carries its own additional complications that make taking care of this patient population more challenging.

Based on our experience with this patient, we identified key areas in the planning and execution of a safe anesthetic technique for MH patients undergoing cardiac surgery:

Preoperative assessment

Establishing the MH susceptibility status is difficult, especially in patients undergoing anesthesia for the first time, as susceptibility is often discovered after exposure to a trigger. It is imperative to review the patients' past medical and family history, including a careful evaluation of the anesthetic records. Careful investigation of hyperthermic reactions particularly in the setting of agents known to trigger MH, in genetically linked relatives may be the first indication of susceptibility. The gold standard for diagnosis can be obtained with the Caffeine Halothane Contracture test, genetic testing is also available. However, these tests take time and may conflict with patient management.

Preparation of the anesthesia machine

It is recommended that anesthesia machines free of residual halogenated anesthetics be used.[3] Newer anesthesia machines have evolved and become more complex; their designs also contain new materials and technologies. Most notably the ventilator and the materials of the internal gas delivery system incorporate more plastic and rubber in unique compositions among newer workstation components. These parts serve as a significant reservoir of anesthetic gas, which is released back into the breathing circuit after anesthetic discontinuation.[4,5] As newer workstations differ in the amount of absorptive materials they use, the amount of time needed to purge them of the volatile gas they store from prior use will differ as well.[6] A study by Petroz *et al*. investigated how absorbent materials within newer anesthesia machines affect the washout times of halothane and isoflurane. The authors compared the Siemens KION workstation against the Ohmeda Modulus I and II machines.[4] The study demonstrated that washout time was more dependent on the type of anesthesia machine rather than the anesthetic agent used when using high fresh gas flow rates (10 l/min).[4]

We paid special attention in preparing the anesthesia machine for our patient to ensure that our methods aligned with the most up to date recommendations found in the literature.[6] The Drager Primus anesthetic machine was utilized for this patient. Preparing the ventilator is accomplished best using the Five-Five-Five-Flush method, the vaporizers and CO_2 absorbent are removed. The old circuit is replaced with a clean one and an activated charcoal filter is inserted at the inspiratory port in the off position. A 2 l artificial lung is also placed. The ventilator is flushed with O_2 10 l/min, V_t 600 ml, respiratory rate 10/min, and I: E ratio of 1:2 for 5 min. Next, the Quick Emergence Device (QED); Anecare Laboratories, Salt Lake City, UT is switched to the on position and O_2 is flushed for another 5 min. The machine is then ready for use. Also it is recommended that the fresh gas flow be maintained at >10 l for the first 5 min of the case.[3]

For this case report, we investigated the protocols used to prepare the anesthesia machines in a systematic review

of published cases of MH susceptible patients undergoing CPB.[7] Out of the 24 cases in the review, 14 patients experienced an MH event, whereas 10 did not.[8-17] Of the 14 patients who experienced MH episodes, 10 were attributed to the use of volatile agents.[18-25] The triggering agent for the other 4 patients remained unknown, however, no known triggering anesthetic agents were used.[26-29]

Of the four cases in which a non-volatile agent associated MH event occurred, none specified the type of anesthesia machine used. The machine preparation parameters, including fresh gas flow rate, and preparation time, were also unreported. This under-reporting impeded our ability to evaluate the adequacy of their methods in flushing the vapor from the machine. Of the 10 event free cases, only 2 could be assessed as having adequately removed the vapor from their machines based on the reported protocols alone. One case reported the type of machine utilized, the fresh gas flow rate, along with the preparation time.[9] The other case did not report the type of machine used, but noted that it was reserved specifically for patients susceptible to MH and thus was free of volatile vapor.[17] There are limited cases on the successful perioperative management of patients susceptible to MH. It is therefore important to not only utilize the few standardized techniques available to prevent adverse events[6], but also important to standardize reporting of protocols to encourage transparency and thorough evaluation.

Anesthetic planning

Classic triggering agents for MH include succinylcholine and all volatile anesthetics (halothane, enflurane, isoflurane, and sevoflurane). However, MH using the volatile anesthetic desflurane has been infrequently reported in humans.[30-33] These agents along with phenothiazines and monoamine oxidase inhibitors should be strictly avoided and if possible removed from the operating room altogether.[1,34] A total intravenous anesthetic regime using propofol, opioids, and non-depolarizing muscle relaxants may be most appropriate. None of these agents have been shown to cause adverse toxic reactions in MH-susceptible patients.[8] It is noteworthy to mention that the incidence of MH crisis is thought to be less in individuals of black African descent.[35-39] A case report of a 28-year-old African American male with prior uneventful anesthetic treatment with isoflurane reported an MH event in a subsequent maxillofacial procedure utilizing desflurane.[35] Further research is necessary in this patient population, especially the unique interplay with the volatile anesthetic desflurane.

Cardiac monitors including continuous mixed venous oxygenation and continuous cardiac output are recommended in addition to standard ASA monitors. In the perioperative period, from induction to the first few days in the postoperative ICU, it is important for the clinician to remain vigilant for the early and late signs of MH. Early signs include hemodynamic instability, tachycardia, metabolic acidosis, rigor, hyperthermia, and hypercapnia.[7] Hyperthermia can occur at any point, early or late, throughout the evolution of an MH crisis but often is not the presenting symptom. In fact, in general, hyperthermia is a rather late sign in an episode of MH.[7] Because end-tidal CO_2 is not measured during CPB, frequent blood gas measurements can aid in early detection of rising CO_2 levels.

It is recommended that MH-susceptible patients undergo slow, careful rewarming to avoid core body temperatures >36°C.[40] It has been shown that physical activity in a hot, humid environment can trigger MH in human beings. It has also been shown that MH can be induced by heat alone in susceptible pig models.[41] Similarly, exogenous heat during rewarming of the patient after hypothermic CPB may also trigger MH in MH-susceptible patients.[21] This has been demonstrated in a patient with a family history of MH who was cooled to a temperature of 32°C during CPB; MH was triggered within 1 hour postoperatively and was attributed to active rewarming.[29]

Hypothermia during CPB creates unique challenges while monitoring for MH since it may mask any rise in body temperature. Hypothermia for cardiac surgery in general, is being questioned. In a prospective, randomized study of 140 patients with valvular heart disease, with or without CAD who were randomly allocated to undergo hypothermic (31-32°C) or normothermic (>36°C) CPB. There was no significant difference in Troponin I levels between the groups.[42] Accurate diagnosis of an MH during CPB requires a high index of suspicion and close monitoring of surrogate markers of MH such as peripheral mottling, cyanosis and sweating.[21] Specifically, in patients who are at high risk for MH, it may be prudent to maintain normothermia during CPB.

Use of inotropic agents

There has been some concern that exogeneous catecholamines can be a factor, increasing the speed of onset, increasing the severity and serving as a primary trigger of MH.[43] These concerns have not been validated in any animal or human studies and it is probably safe to use them as needed.

Delayed onset MH

Hari *et al*. reported a delayed onset MH in a 35-year-old male who underwent a right carpal bone fracture fixation, 3 days after a general inhalational anesthetic.[44] This case demonstrated the need for continued surveillance in the immediate and extended postoperative period for MH-susceptible patients. In our case, we continued monitoring for MH throughout her ICU and hospital stay to ensure the patient remained MH symptom free.

Prophylactic dantrolene

Prophylactic treatment of MH susceptible patients with dantrolene has been questioned as early as 1990. In a review

of 30 cases, prophylactic dantrolene was withheld and all patients remained symptom free. The authors concluded that dantrolene is not necessary and recommended close monitoring for signs of MH.[45] Furthermore, it has been postulated that prophylactic dantrolene may mask early symptoms and possibly delay full treatment.[24] Dantrolene use poses its own risk, such as prolonged muscle weakness.

Alternate surgical techniques

CPB causes a systemic inflammatory response, which could potentially trigger MH. It has been recommended that, if feasible, CPB be avoided by resorting to off-pump techniques when only CABG is required.[24]

Conclusion

The risk of triggering MH in susceptible patients continues to be a major concern during cardiac surgery. Close communication between all members of the cardiac team including, surgeon, perfusionists, anesthesia technicians and intensivists is vital. Apart from meticulous preparation of the anesthetic machine, avoidance of triggering agents and close monitoring, other important measures while managing these patients are as follows: avoidance of hypothermia during CPB, slow rewarming after CPB, "off-pump" CABG if possible, continued high-level vigilance throughout the postoperative period and immediate availability of dantrolene. Though it is not conclusive, certain exogenous catecholamines may trigger MH so it may be prudent to use only small doses as needed. Also, prophylactic dantrolene is not recommended. Ultimately, early detection, high index of clinical suspicion and immediate treatment with dantrolene will decrease overall morbidity and mortality associated with MH. There is a low incidence of MH complications due to the rarity of its genetic cause, clear and thorough reporting from clinicians of MH events will continue to improve management strategies to ensure that patients receive the best standard of care.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due diligence will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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