

A Suspected Case of Delayed Onset Malignant Hyperthermia with Desflurane Anesthesia

Thomas J. Papadimos, MD, MPH, Mohamad Almasri, MD, James C. Padgett, CRNA, BS, and Joanne E. Rush, CRNA, MS

Department of Anesthesiology, Medical College of Ohio, St. Luke's Hospital Heart Center, Maumee

Desflurane has been identified as a weak triggering anesthetic of malignant hyperthermia that, in the absence of succinylcholine, may produce a delayed onset of symptoms. The prolonged interval after exposure may occur more than 6 h after the induction of anesthesia.

The unintended underdosing of this patient with dantrolene and the prompt reversal of symptoms may be an attribute of the genetic expression of a weak triggering volatile anesthetic such as desflurane.
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Malignant hyperthermia (MH), an anesthetic-related disorder of skeletal muscle calcium regulation, is triggered by succinylcholine and volatile anesthetics. It is characterized by hyperthermia, tachycardia, acidosis, and muscle rigidity (1). Several reports indicate that MH symptoms can become manifest after a prolonged exposure interval when desflurane is the only trigger (2-6). We report a case of suspected delayed onset MH during thoracotomy in which desflurane was the sole trigger.

Case Report

A 56-yr-old man presented for a right thoracotomy and tumor excision. His medical history included atrial fibrillation, chronic obstructive pulmonary disease, hypertension, tobacco, and excessive alcohol use. He had had a tonsillectomy as an adult without anesthetic complication and denied any allergies. His medications included ramipril, amiodarone, carvedilol, coumadin, and Percocet.

Preoperative physical examination revealed a well-nourished 80-kg man, 172 cm in height. Preoperative vital signs were: arterial blood pressure, 148/66 mm Hg; heart rate, 63 bpm; oxygen saturation, 95%, with a fraction of inspired oxygen (F_{iO_2}) = 0.2; and oral temperature, 37.0°C. Hemoglobin and hematocrit were 13 g/dL and 40%, respectively. Coumadin had been discontinued before surgery, and coagulation studies were acceptable. Cardiopulmonary examination revealed a regular rhythm without murmurs, and rhonchi were audible in the right upper lung fields. Chest radiograph and computerized tomography confirmed the mass.

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Address correspondence and reprint requests to Thomas J. Papadimos, MD, 7162 Copperwood Lane, Sylvania, Ohio 43560. Address e-mail to TPapadimos@mac.com.

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The patient was premedicated with 2 mg of midazolam IV. A thoracic epidural and a left radial artery catheter were placed. After breathing 100% oxygen, anesthesia was induced with 250 μ g of fentanyl IV, 200 mg of propofol IV, and 100 mg of lidocaine IV. After giving rocuronium 60 mg IV, a #37 left-sided double-lumen tube was inserted, and proper positioning was confirmed fiberoptically (both in the supine and left lateral decubitus position). Anesthesia was maintained with desflurane (range, 5-8 minimum alveolar anesthetic concentration) in oxygen with fentanyl boluses accompanied by additional rocuronium. The arterial blood gas (ABG) before one-lung ventilation was pH 7.36, P_{aCO_2} 43 mm Hg, P_{aO_2} 475 mm Hg, base excess -0.7 mmol/L, HCO_3^- 24.5 mmol/L, and minute ventilation was 9 L/m. This minute ventilation was used for the first 300 min of anesthesia, which included the first 190 min of one-lung ventilation. The soda-lime canister was changed after the induction of anesthesia because color change indicated exhaustion. Between 300 and 335 min after the induction of anesthesia (190-225 min of one-lung anesthesia), the heart rate increased from 70 to 85 bpm, the end-tidal CO_2 ($ETCO_2$) increased from 44 to 53 mm Hg, and he remained afebrile. The ABG at this time was pH 7.20, P_{aCO_2} 67 mm Hg, P_{aO_2} 379 mm Hg, base excess -1.2 mmol/L, and HCO_3^- 25 mmol/L. Venous CO_2 was not measured. Minute ventilation was increased to 12 L/m, and gradually increased to 22 L/m (see below), and proper double-lumen tube placement was reconfirmed fiberoptically. The valves on the anesthesia machine were checked and were in working order. There were no significant changes in peak inspiratory pressures throughout the case.

At 395-min postinduction of anesthesia, during chest closure, while on two-lung ventilation (the double-lumen tube had been pulled back into the trachea and both lungs visibly expanded well), the heart rate increased to 120 bpm, $ETCO_2$ increased to 80 mm Hg, and nasopharyngeal temperature increased to 38.9°C. The ABG was pH 7.16, P_{aCO_2} 92 mm Hg, P_{aO_2} 224 mm Hg, potassium 5.0 mmol/L, and minute ventilation was 22 L/m. MH was presumed, and desflurane administration was terminated. Dantrolene was given IV

(retrospectively, it was discovered that half of the recommended dose of 2.5 mg/kg was given). The anesthesia machine was replaced with a Puritan-Benett 840 ventilator for the final 35 intraoperative min (430 total postinduction min). Propofol and fentanyl were used to ensure amnesia and analgesia. The patient was also packed with ice. The patient improved immediately with dantrolene; heart rate was 90 bpm, ETCO_2 54 mm Hg (Paco_2 58 mm Hg; pH value of 7.35), and he became normothermic. The patient was moved to the intensive care unit, and dantrolene administration was inadvertently discontinued. Copious diuresis was ensured with furosemide and mannitol. Creatine phosphokinase was 2264 U/L after surgery and peaked at 4650 U/L 12 h later. Renal function was never compromised, and urine myoglobin levels were negligible. Thyroid function studies and cardiac enzymes were normal. The patient recovered uneventfully. He was counseled about MH and referred appropriately for diagnostic testing.

Discussion

Desflurane can trigger MH without the use of succinylcholine and may produce a delayed onset. This patient's symptoms were delayed over six hours. The patient had a clinical grading scale of 43 (grade D5). Grades D5 (very likely) and D6 (almost certain MH) are defined by scores of 35–49 and ≥ 50 , respectively (7). The clinical grading scale uses six process indicators and a seventh "other" category indicator: rigidity, muscle breakdown, respiratory acidosis, temperature increase, cardiac involvement, family history, and "indicators not part of a single process" with 3–15 points awarded to subcategories of each indicator. Our patient was scored as follows: (a) arterial $\text{Paco}_2 > 60$ mm Hg with appropriately controlled ventilation (15 points), (b) inappropriately increased temperature $> 38.8^\circ\text{C}$ in the perioperative period (10 points), (c) inappropriate sinus tachycardia (3 points), (d) arterial pH value < 7.25 (10 points), and (e) rapid reversal of MH signs of metabolic or respiratory acidosis with IV dantrolene (5 points). The increase in temperature was rapid (15 points), but the more conservative inappropriate increase in temperature category (10 points) was chosen; both left the patient as a D5.

Whereas Wedel et al. (2) demonstrated weaker triggering by desflurane than halothane in susceptible swine, it is interesting that there was no evidence for graded, slow onset triggering. The triggering, once started, was sudden. Further work by Allen and Brubaker (4) indicated that presentation of MH with desflurane use (without succinylcholine) may be delayed (53–380 minutes), and they also suggest that desflurane is a weak trigger. Several case reports are in agreement that, without succinylcholine exposure, desflurane causes delayed-onset MH (3,5,6).

Our patient had no other triggers but desflurane. The dramatic temporal response to dantrolene suggests this was indeed an MH event. Such a response to

an unintended half dose of dantrolene may be representative of a weak triggering drug. In one report of desflurane-triggered MH, a suboptimal dose was given two hours after diagnosis with good result (the patient was in a remote location) (3). Whereas various anesthetics may trigger MH at different speeds, two important factors that may affect such triggering should not be overlooked. First, it must be noted that graded doses of dantrolene modify an MH porcine episode: 3 mg/kg, signs of MH still are detectable; 1 mg/kg, MH definite, but attenuated; and 0.1 mg/kg, no effect of dantrolene on MH (8). Second, depressants and nondepolarizing muscle relaxants delay the onset of MH in pigs (9). For example, a pig subjected to an inhaled induction with halothane triggers within three minutes. If the same pig is given a sleep dose of thiopental and then given halothane, the onset is 20 minutes. Therefore, should MH be diagnosed during desflurane anesthesia, it is of paramount importance that the recommended dose of 2.5 mg/kg of dantrolene be used. Nonetheless, this case raises the question of the relative lethality of desflurane as the sole trigger of MH, and it is a fascinating prospect to engineer or design an absence of MH risk into a drug. More investigation is required regarding delayed onset MH caused by weak triggering drugs and atypical presentations in light of the multiple MH genetic variations at the ryanodine receptor (10).

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