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Short Report

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A Case of Malignant Hyperthermia During Sevoflurane Anesthesia

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Malignant hyperthermia (MH) is a chain reaction of symptoms that is triggered in susceptible individuals by commonly used inhalation agents such as halothane, enflurane and isoflurane, and the muscle relaxant succinylcholine. The symptoms include a greatly increased body metabolism, muscle rigidity and high fever. During sevoflurane anesthesia, we encountered a case of MH, which was successfully treated by symptomatic treatment.

Case Report

A 23-year-old, 55-kg man was scheduled for nasoplasty because of septonasal deformity. Neither the patient nor his family had any history of neuromuscular disease, and he had not received general anesthesia previously. Preoperative laboratory examinations were within normal values.

The patient did not receive premedication. Anesthesia was induced with the intravenous administration of thiopental (500 mg), fentanyl (50 µg) and vecuronium (8 mg), and an 8.5 mm tracheal tube was inserted without any difficulty under direct laryngoscopy. Anesthesia was maintained with sevoflurane 1.5-2% in 65% nitrous oxide/35% oxygen at a flow rate of approximately 4 and 2 L/min, respectively. Standard monitoring was used, but end-tidal CO_2 was not monitored during anesthesia in this case because no capnograph was available. Before induction of anesthesia, heart rate and systolic/diastolic blood pressure were 94 beats per minute and 110/80 mmHg. Rectal temperature after the induction of anesthesia was 36.9ºC. One hundred ten minutes after induction, adrenaline (4 ml, 1:200000) and prilocaine (4 ml, 2%) were injected submucosally by the surgeon to reduce bleeding and for early postoperative pain relief. Vital signs remained stable for 120 minutes after induction when the patient suddenly developed a tachycardia of 148 beats per minute. The increasing heart rate was considered to be due to local anesthetic containing adrenaline, but rectal temperature also increased dramatically, from 36.9 to 39.9ºC in 15 minutes, and profuse sweating was noted. There was marked skeletal muscle rigidity of the upper and lower extremities. Soda lime absorber was noted to be hot, and its color changed to purple. We concluded that malignant hyperthermia had developed; sevoflurane and nitrous oxide were discontinued, and 100% oxygen was administered through the same anesthetic circuit at a high flow rate (12 L/min). The operation was terminated as soon as possible, and active cooling was immediately initiated by ice water. A 16-gauge femoral venous and a 20-gauge right arterial catheter were inserted. At that time, pH was 7.15, PaO_2 479 mmHg, $PaCO_2$ 64 mmHg, base excess -9 mmol/L, and potassium 4.3 mEq/L. Severe hypercarbia was in no way associated with rebreathing or inadequate ventilation. Sodium bicarbonate, verapamil, methyl prednisolone and insulin-5% dextrose solution were administered intravenously. Furosemide and 20% mannitol infusion were given for adequate urine output. Midazolam was given for sedation. Muscle rigidity improved slowly over the next 50 minutes. During active

cooling, ventricular tachycardia of five seconds duration developed, and bolus dose lidocaine was given initially, followed by infusion. When the rectal temperature decreased to 38.5ºC, active cooling was terminated. Approximately 2 hours after the onset of MH, the patient was responsive and demonstrated adequate muscle strength, and the trachea was extubated. Analysis of arterial blood revealed a pH of 7.39, $PaCO_2$ 54 mmHg, PaO_2 115 mmHg, base excess +6 mmol/L, and potassium 3.6 mEq/L. The patient was transferred to the intensive care unit for further observation. Dantrolene was not administered, as it was not available when the attack developed. The serum creatine phosphokinase level reached a maximum value of 4138 IU/L at the 24th postoperative hour and began to decrease on the second postoperative day. The blood myoglobin concentration was >405 ng/mL at the fifth postoperative hour, and returned to normal on the second postoperative day. The postoperative period was uneventful and the patient was discharged from the hospital five days after the operation.

Three factors may have contributed to the rapid rise in temperature seen in our patient: sevoflurane, prilocaine and adrenaline. It was previously believed that amide local anesthetics could trigger MH (1). Support for this hypothesis was provided by a report of an MH episode occurring during epidural anesthesia with lidocaine, suggesting that the amide local anesthetics in large doses might trigger MH (2). On the other hand, in inbred swine, MH is not triggered even with enormous doses of intravenous lidocaine (3). In addition, another amide local anesthetic, prilocaine, has been used for the contracture test under 3-in 1 lumbar plexus blockade for the diagnosis of MH in several studies, and it was suggested that prilocaine is a safe drug in MH susceptible patients (4). Finally, amide local anesthetics are now routinely used for nerve blockade anesthesia in MH susceptible patients undergoing muscle biopsy, without untoward events. In our patient, we also used prilocaine and lidocaine, amide local anesthetics, for postoperative analgesia and treatment of MH in ventricular tachycardia attack, respectively. We believe that neither of these agents was responsible for the development of MH in our patient, as prilocaine is a safe agent and lidocaine was used in low doses.

It has been suggested that sympathetic activity contributes to fulminant MH syndrome (5). In our case, adrenaline administration 10 minutes prior to the MH crisis might have been the initiating agent. However, it has been shown that continuous intravenous infusion of noradrenaline in pigs in blood concentrations of as high as 140 ng/ml did not mediate or initiate the porcine whole body stress response characteristic of MH (6). At present, it is widely accepted that adrenaline is a safe drug for MH susceptible patients and therefore is an unlikely candidate for the initiating agent in our patient.

Shulman et al. reported that sevoflurane triggered MH in MH susceptible swine, but the relationship between MH and sevoflurane is not well defined in humans (7). The onset of MH with sevoflurane in humans has been reported to occur both at an early period and after prolonged anesthesia (8). In our patient, the MH crisis developed 2 h after inhalation of sevoflurane, and we believe that in the present case the initiating agent was sevoflurane. The symptoms in our case were mild and did not persist after sevoflurane discontinuation, and, despite the unavailability of dantrolene, responded well to symptomatic treatment. There are five case reports in which benign sevoflurane induced MH occurred and was treated with dantrolene.

Dantrolene inhibits intracellular calcium release by the sarcoplasmic reticulum and dissociates excitation-contraction in muscle cells. Although intravenous administration of dantrolene is a specific therapeutic agent for MH, we were not able to use dantrolene because it was not available in the early stage. Dantrolene was obtained eight hours after the occurrence of MH but, since the patient recovered, it was not used. To the best of our knowledge there has been no previous report of sevoflurane-induced MH treated without dantrolene.

Calcium channel blockers such as verapamil are not recommended in MH crises since hyperkalemia may occur with the dantrolene-verapamil combination, as has been previously reported in both animals and humans (10). However, San Juan et al. showed in an animal model that the increase in potassium could be totally attributed to intravenous dantrolene alone (10). As no dantrolene was administered to our patient, we used verapamil for supraventricular tachycardia, and the peak serum potassium level did not exceed 4.3 mmol/L.

This case report shows that MH triggered by sevoflurane is mild. Although dantrolene is essential for the management of MH, when it is unavailable, mild MH may be treated with vigorous management of symptoms.

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