

Anesthesiology
60:149-150, 1984

Malignant Hyperthermia during a Prolonged Anesthetic for Reattachment of a Limb

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Malignant hyperthermia is a genetically determined syndrome characterized by hypercatabolic reactions of skeletal muscle. There exists a wide variation in its clinical presentation.¹ Many people susceptible to malignant hyperthermia escape detection; many even have undergone surgery and anesthesia without triggering the syndrome.^{2,3} The following case involves three anesthetic inductions and a prolonged inhaled anesthetic exposure (26½ h) during the 36 h prior to the development of malignant hyperthermia.

REPORT OF A CASE

A previously healthy 19-year-old (60 kg) man sustained extensive injury to his left axilla during a fall through a window. Following an oral endotracheal intubation under fentanyl sedation, a 3-h general anesthetic utilizing oxygen, nitrous oxide, enflurane, pancuronium, and fentanyl was uneventful. Arterial blood pressure was 120/60 mmHg, heart rate 85-100 beats/min and temperature 37° C orally. During surgery, all major structures in the left brachial neurovascular bundle were severed. The decision was made to terminate the procedure and transfer the patient to our hospital.

Upon arrival in the operating room, arterial blood pressure was 120/75 mmHg, heart rate 80 beats/min, and oral temperature 35° C. After *d*-tubocurarine 3 mg iv, anesthesia was induced with thiopental 350 mg iv. Oral endotracheal intubation was accomplished easily following succinylcholine 120 mg iv. For 21 h, anesthesia was maintained with nitrous oxide, 4.0 l·min⁻¹, and oxygen 2.0 l·min⁻¹, enflurane 0.75-1.5%, morphine 29 mg iv, thiopental 700 mg iv, and *d*-tubocurarine 24 mg iv. The heart rate varied between 70 and 110 beats/min⁻¹, arterial blood pressure between 110/70 and 150/80 mmHg, and esophageal temperature between 35° C and 37° C. During the 20th hour of surgery, with a FI_O₂ of 0.3, the Pa_O₂ was 139 mmHg, Pa_{CO}₂ 45 mmHg, and pH_a 7.37. The trachea was extubated uneventfully at the end of the surgical procedure.

Postoperatively the patient had a persistent tachycardia of 120 beats/min. Oral temperature was 37° C. With a FI_O₂ of 0.21, the Pa_O₂ was 82 mmHg, Pa_{CO}₂ was 42 mmHg, pH_a 7.49. Eight hours postoperatively,

his left hand was noted to be cold and pulseless. Surgical reexploration was rescheduled immediately.

On arrival in the operating room, he complained bitterly of pain in his right arm and abdomen. The fingers on his right hand where the intravenous and radial artery cannulae had been inserted were pink and warm. There was no evidence of either inflammation or infiltration of intravenous fluid. However, attempts to change arm position and move the patient to the operating table were accompanied by cries of pain. Physical examination of the abdomen by the surgeon was felt to be negative. The patient was sedated with morphine 10 mg IV with relief of pain.

The trachea was reintubated easily after administration of *d*-tubocurarine 6 mg iv, thiopental 260 mg iv, and succinylcholine 120 mg iv. Anesthesia was maintained with nitrous oxide 3.0 l·min⁻¹, oxygen 3.0 l·min⁻¹, and halothane 0.75-1.0% (delivered by a Fluotec vaporizer). Ventilation was controlled. Heart rate and arterial blood pressure were 80 beats/min and 120/70 mmHg, respectively. The esophageal temperature was 37° C. The central venous pressure, which had been 5-8 cmH₂O postoperatively in the recovery room and 19 cmH₂O prior to induction of anesthesia, remained elevated at 22 cmH₂O. The urine output was brisk (400 ml/h). Because the hematocrit was 22%, two units of packed erythrocytes were infused slowly during the first 2 h of the procedure. During this time the previously normal arterial wave form became abnormal in that it was followed by a second wave of lesser amplitude. Arterial blood gases with a FI_O₂ of 0.5 were Pa_O₂ 181 mmHg, Pa_{CO}₂ 31 mmHg, and pH_a 7.56. Fifteen minutes later, the temperature rose to 38° C, and adequate ventilation was difficult to achieve. The heart rate rose to 160 beats/min and the arterial blood pressure to 260/90 mmHg. Anesthesia was discontinued except for the administration of 100% oxygen. Surgery was stopped and the drapes removed from the patient's head and body, revealing marked pectoral and masseter muscle rigidity causing occlusion of the endotracheal tube. A central venous blood gas revealed a P_O₂ of 45 mmHg, P_{CO}₂ 56 mmHg, and a pH 7.28 (FI_O₂ = 1.0). Ventilation was controlled with a FI_O₂ of 1.0 using a different anesthetic machine. Iced saline was given rapidly iv and via gastric lavage. Sodium bicarbonate 88.6 mEq was administered iv. Fifteen minutes after the increase in heart rate, the oral temperature was 39.1° C. The patient began to hyperventilate at a rate of 40 breaths/min, emptying the 5 l reservoir bag with each breath. With a FI_O₂ of 1.0, the Pa_O₂ was 248 mmHg, Pa_{CO}₂ 50 mmHg, pH_a 7.31; venous blood gases were P_O₂ 42 mmHg, P_{CO}₂ 65 mmHg, pH 7.22; serum potassium was 4.1 mEq/l. Dantrolene 180 mg (3 mg·g⁻¹) was administered iv. During the next 20-30 min the temperature decreased to 37.5° C, the heart rate to 80 beats/min, and the arterial blood pressure to 140/70 mmHg; and the muscular rigidity resolved.

Anesthesia was resumed with droperidol 10 mg iv, morphine 10 mg iv, O₂ 6.0 l·min⁻¹ and N₂O 6.0 l·min⁻¹. Thirty minutes later with a FI_O₂ of 0.5, the Pa_O₂ was 62 mmHg, Pa_{CO}₂ 43 mmHg, and pH_a 7.44. The central venous pressure was 26 cmH₂O. Furosemide 20 mg was given iv, and 5 cmH₂O of peak end-expiratory pressure was established. With a FI_O₂ of 0.5, Pa_O₂ was 146 mmHg, Pa_{CO}₂ 31 mmHg, and pH_a 7.50. The central venous pressure was 17 cmH₂O. The surgical procedure was completed without further incident. A tachycardia accompanied by hypertension during emergence was treated successfully with 5 mg droperidol iv and 5 mg morphine iv.

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Received from the Department of Anaesthesia, Harvard Medical School, Boston, Massachusetts, and the Department of Anesthesiology, Massachusetts General Hospital, Boston, Massachusetts. Accepted for publication June 29, 1983.

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Key words: Anesthesia: duration. Hyperthermia: malignant.

Four hours after admission to the ICU, the patient experienced transient stiffness of the legs accompanied by an oral temperature rise to 39° C. Droperidol 5 mg iv and morphine 5 mg iv were given. This resulted in alleviation of symptoms and a decrease in temperature. Twenty-four hours postoperatively and 30 min prior to extubation of the trachea, 60 mg of drantolene was given iv (1 mg · kg⁻¹). Extubation of the trachea was performed without incident.

The patient's CPK at the time of admittance to the ICU was 1,500 units (normal range in our lab is 5–55 units) and 48 hours postoperatively was 1,296 units. Urine myoglobin also was positive 24 hours postoperatively.

DISCUSSION

The mechanisms that trigger malignant hyperthermia in humans are not known. The hypercatabolic crisis usually occurs suddenly and with little warning. It can be precipitated by inhaled anesthetics, both depolarizing and nondepolarizing neuromuscular blocking agents, amide local anesthetics, and by other stresses. A history of an uneventful anesthetic does not guarantee a patient's safety in subsequent anesthetics.

In this case, the patient underwent uneventfully three separate anesthetic inductions and was exposed to known triggering agents for a total of 26½ hours within a 36-h period of time before developing signs of the syndrome. The patient then developed a rapid progression of marked muscular rigidity, rise in temperature, tachycardia, tachypnea, hypertension, acidosis, and increased oxygen utilization. Successful therapy included cessation of anesthesia and surgery, cooling of the patient's body (intravenous, intragastric, and surface cooling were employed), and administration of 100% oxygen, sodium bicarbonate iv, furosemide iv, and dantrolene 3 mg · kg⁻¹ iv. The decision to continue surgery was based on the patient's response to intravenous dantrolene and the consequences of not completing this particular surgery.

There were several occurrences in this case that cannot be explained easily. The development of arm and abdominal pain on transfer back to the operating room did not have a clear cause. There was no evidence of phlebitis or arterial spasm, and he did not show signs of an acute process in his abdomen. Intravenously administered morphine did cause a dramatic cessation of this pain. Perhaps this event represented the initial evidence of malignant hyperthermia.

The elevation in central venous pressure on return to the operating room was also troublesome. Since this was a persistent reading, we accepted it as being real. Perhaps it was associated with hypervolemia secondary to excessive administration of crystalloids. The patient also experienced a persistent profound diuresis of unknown cause. Possible causes of this diuresis include iv administered dextran-40, started during the previous anesthetic, and the prolonged enflurane anesthetic itself. Subsequent to

this brisk diuresis, the patient had metabolic alkalosis. Despite this metabolic alkalosis, sodium bicarbonate was administered iv upon the development of muscular rigidity because of the known rapid development of profound metabolic acidosis accompanying malignant hyperthermia.

The appearance of a "hyperdynamic" arterial wave form, *i.e.*, a secondary peak of lesser amplitude immediately following the initial arterial wave, is noteworthy. We have seen this in other hyperdynamic states such as hypercarbia and sepsis in young people. The development of this wave form was dramatic and occurred about 15–20 minutes prior to the onset of muscular rigidity, tachycardia, and hyperthermia.

There is no simple noninvasive screening test for malignant hyperthermia prior to surgery. Susceptible patients can demonstrate an elevated serum CPK preoperatively. Once the syndrome has occurred, the CPK may be elevated markedly, as seen with this patient postoperatively.

There are certain characteristics common to many susceptible individuals: muscular cramping, joint hypermobility and dislocation, scoliosis, ptosis, and squint.⁴ Postoperative interviews with this patient and his family revealed a history of both severe leg cramps and "tightness of the chest wall" in both the patient and his father.

Approximately 10% of patients who develop the syndrome of malignant hyperthermia show signs of recurrence in the first 24 hours postoperatively.⁵ This patient developed two episodes of recrudescence, one on emergence from his neurolept anesthetic and one 4 h after admission to the ICU. Both episodes appeared to be attenuated by the use of droperidol and morphine sedation, allowing time to prepare the dantrolene solution for administration if the "full-blown" syndrome had redeveloped.

In conclusion, this case illustrates that there is no time when a person who is susceptible to developing malignant hyperthermia is safe from "triggering" the syndrome.

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