CASE REPORT

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Malignant hyperthermia: a case report with a literature review

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Malignant hyperthermia is an extremely rare, potentially lethal disorder that occurs in susceptible patients who are exposed to triggering agents such as volatile anesthetic gases or depolarizing muscle relaxants. The clinical manifestations of malignant hyperthermia include hypermetabolism, hyperthermia, hypercapnia, and sustained skeletal muscle rigidity, which result in cardiac arrest, brain damage, and death. It is associated with a high morbidity and mortality rate if not recognized immediately and treated appropriately. We report a case of suspected malignant hyperthermia in a young male patient undergoing axillary osmidrosis surgery.

Keywords Malignant hyperthermia / General anesthesia / Intraoperative awareness / Case reports

INTRODUCTION

Malignant hyperthermia is a rare but life-threatening condition that occurs in susceptible patients who are exposed to specific triggering agents such as volatile anesthetic gases (e.g., sevoflurane, isoflurane, or desflurane) or depolarizing muscle relaxants (succinylcholine) [1]. Although the exact epidemiology of malignant hyperthermia is unknown, its incidence is estimated to range from approximately 1:100,000 to 1:500,000 in anesthesia procedures [2,3]. Susceptibility to malignant hyperthermia is an autosomal dominant disorder that involves mutations in the type 1 ryanodine receptor (*RYR1*) gene, which is mostly expressed in skeletal muscle [4]. As ryanodine receptors are essential for excitation-contraction coupling, mutations in the *RYR1* gene disrupt excitation-contraction coupling and lead to enhanced calcium ion release from the sarcoplasmic reticulum of skeletal muscle in response to triggers [5]. These calcium ions, which are released in abnormal abundance from the sarcoplasmic reticulum, bind to the myofilament, resulting in dysregulated skeletal muscle contraction. This contractile state leads to muscle rigidity, breakdown, and hypermetabolism, with signs including acidosis, hyperthermia, hypercarbia, and increased serum creatine kinase concentration [6]. A delay in early recognition and appropriate treatment can result in complications such as cardiac arrest, renal failure, compartment syndrome, disseminated intravascular coagulation, and death [1,6]. We report a case of suspected malignant hyperthermia in a healthy young male patient during an operation for axillary osmidrosis, which we identified promptly based on laboratory findings and successfully treated intraoperatively.

CASE REPORT

A 20-year-old man presented to our hospital for circumcision and a bilateral axillary subdermal excision operation. He had no past medical history and no known drug allergies. He did not have any previous anesthetic exposure and there was no family history of problems with anesthesia. Surgery was performed in collaboration with the urology department under general anesthesia, as the patient was worried about pain during surgery. General anesthesia was induced with propofol and rocuronium, and then maintained with desflurane. The patient's initial vital signs were reported to be stable, with a blood pressure of 122/59 mmHg, heart rate of 86 beats per minute, respiratory rate of 18 breaths per minute, oxygen saturation of 100%, and a temperature of 36.3°C. Approximately 1 hour

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into surgery, two important events were noticed. First, the patient's body temperature had increased to 37.6°C, and second, the patient's partial pressure of carbon dioxide (PCO_2) had increased to 49.6 mmHg. Initially, a circuit check and adjustment in minute ventilation were done, but the PCO_2 continued to rise to 55 mmHg and hyperthermia continued to be observed without a specific focus. The patient's heart rate and blood pressure had also risen, with maximum readings of 126 beats/min and 150 mmHg, respectively. The arterial-blood gas analysis at this time showed the following results: pH, 7.28; PCO_2, 50.2 mmHg; partial pressure of oxygen (PO_2), 339 mmHg; base excess, –4 mEq/L; and HCO_3, 23.6 mEq/L. These findings were suggestive of mixed respiratory and metabolic acidosis. With the consistent hypercapnia, hyperthermia, and hypermetabolism, malignant hyperthermia was strongly considered. Because dantrolene was not available in our hospital, we called an adjacent medical center that possessed this drug and requested them to deliver it to us as quickly as possible. Desflurane inhalation was stopped and switched over to total intravenous anesthesia. Active cooling was started with cold saline intravenously, and bladder irrigation through a Foley catheter was done. The blanket covering the patient was removed, and ice packs and cold towels were used for surface cooling. Dantrolene, which is the drug of choice for malignant hyperthermia, could not be used because our hospital did not have the drug in stock. Upon discontinuation of inhalation gas and active cooling, the patient had an adequate clinical response with resolution of tachycardia, hyperthermia, and an improvement in PCO_2 to 35 mmHg. The dantrolene arrived from the other medical center, but we decided not to use it because the patient's acute symptoms had improved. Surgery was completed safely within 1 hour and the patient was transferred to the intensive care unit. The postoperative laboratory findings showed an elevated creatine kinase level of 13,708 U/L, supporting the diagnosis of malignant hyperthermia. During 4 days of postoperative management, the patient's PCO_2, temperature, and acid-base status returned to normal, and his creatine kinase level began to trend downward. He was discharged in a stable condition and was made aware of the suspected diagnosis of malignant hyperthermia and the risk of recurrence upon future exposure to anesthesia.

DISCUSSION

Malignant hyperthermia is a rare but life-threatening condition that occurs in susceptible patients who are exposed to specific triggering agents such as volatile anesthetic gases. It is associated with a high morbidity and mortality rate if not recognized immediately and treated appropriately [1]. For the gold-standard diagnostic test for malignant hyperthermia, a freshly biopsied muscle tissue sample is required and an *in vitro* halothane caffeine contraction test is used. In this test, malignant hyperthermia susceptibility is detected via the response of live muscle specimens to caffeine or halothane [7]. However, this contracture test is not widely available, time-consuming, expensive, and invasive, and it requires a specialized testing center with trained personnel. Furthermore, clinicians cannot wait for a contraction test result in the face of an acute malignant hyperthermia event. DNA analysis is an alternative diagnostic method for malignant hyperthermia susceptibility. It is non-invasive, requiring only a small blood sample for the test, and it can be evaluated in patients of any age and weight [1]. In 50%–70% of families, *RYR1* is the gene responsible for malignant hyperthermia. However, multiple genes are responsible for this condition, and many pathogenic variants may exist; the genetic cause is unknown in the other 30%–50% of families affected by malignant hyperthermia. For this reason, genetic testing cannot exclude susceptibility to malignant hyperthermia; the *in vitro* halothane caffeine contraction test remains the gold standard for testing individuals [7]. Because of these drawbacks, the diagnosis of malignant hyperthermia must be made on the basis of the clinical presentation in most cases, and the clinical grading scale has been widely and effectively used for the differential diagnosis of suspected malignant hyperthermia patients. Larach et al. [8] developed the clinical grading scale for malignant hyperthermia using several patient parameters during the event (Table 1). This raw score is designed to rank suspected patients from 1 ("almost never malignant hyperthermia") to 6 ("almost certain malignant hyperthermia") (Table 2). In our case, the patient had a score of 63 points, where a score of >50 points means "almost certain" for a diagnosis of malignant hyperthermia (Table 3).

The drug of choice for a malignant hyperthermia crisis is intravenously administered dantrolene [9]. Prior to the discovery of dantrolene, the mortality rate of malignant hyperthermia was approximately 80%. The mortality rate has been reduced to approximately 5% after the introduction of dantrolene into clinical practice [10]. Dantrolene binds to the *RYR1* receptor and inhibits the release of calcium from the sarcoplasmic reticulum of skeletal muscle. As the intracellular calcium level decreases, dantrolene reverses the effects of malignant hyperthermia [11]. The recommended dose of dantrolene is 2.5 mg/kg every 5 to 10 minutes until the signs of malignant hyperthermia are controlled. If there is no sign of response, a total dose of up to 10 mg/kg is recommended. However, after administering 10 mg/kg of dantrolene, hyperthermia, acidosis, and muscle rigidity do not resolve, the differential diagnosis should be evaluated [12].

In addition to dantrolene, treatment of malignant hyperthermia includes discontinuation of the triggering agents, active cooling, and stopping the surgical procedure if needed. As soon as a clinician makes a diagnosis of malignant hyperthermia, the administration of all triggering agents must be stopped, and switching to total intravenous anesthesia is recommended. This case report highlights the importance of awareness of malignant hyperthermia and its presentation. Unexplained hypercapnia and hyperthermia during anesthesia are the most common signs of malignant hyperthermia

Table 1. Malignant hyperthermia clinical grading scale

Process	Indicators	Points
Process I: rigidity	Generalized rigidity	15
	Masseter rigidity	15
Process II: muscle breakdown	Elevated CK > 20,000 U/L (after succinylcholine administration)	15
	Elevated CK > 10,000 U/L (without exposure to succinylcholine)	15
	Cola-colored urine	10
	Myoglobin in urine > 60 μg/L	5
	Myoglobin in serum > 170 μg/L	5
	Blood/plasma/serum K^+ > 6 mEq/L	5
Process III: respiratory acidosis	$P_{ET}CO_2$ > 55 mmHg with controlled ventilation	15
	P_ACO_2 > 60 mmHg with controlled ventilation	15
	$P_{ET}CO_2$ > 60 mmHg with spontaneous ventilation	15
	P_ACO_2 > 65 mmHg with spontaneous ventilation	15
	Inappropriate hypercarbia	15
	Inappropriate tachypnea	10
Process IV: temperature increase	Inappropriately rapid increase in temperature	15
	Inappropriately increased temperature > 38.8°C in perioperative period	10
Process V: cardiac involvement	Inappropriate sinus tachycardia	3
	Ventricular tachycardia or fibrillation	3
Others	Arterial base excess more negative than –8 mEq/L	10
	Arterial pH < 7.25	10
	Rapid reversal of malignant hyperthermia signs of metabolic and/or respiratory acidosis with intravenous dantrolene	5

CK, creatine kinase; $P_{ET}CO_2$, postapneic end-tidal carbon dioxide pressure; P_ACO_2, partial pressure of carbon dioxide in arterial blood.

Table 2. Malignant hyperthermia raw scores and ranks

Raw score range	Malignant hyperthermia rank	Description of likelihood
0	1	Almost never
3–9	2	Unlikely
10–19	3	Somewhat less than likely
20–34	4	Somewhat greater than likely
35–49	5	Very likely
≥ 50	6	Almost certain

Table 3. Malignant hyperthermia score in the patient presented herein

Indicator	Points
Elevated CK > 20,000 U/L	15
$P_{ET}CO_2$ > 55 mmHg with controlled ventilation	15
Inappropriate hypercarbia	15
Rapid increase in temperature	15
Inappropriate tachycardia	3
Total score	63

CK, creatine kinase; $P_{ET}CO_2$, postapneic end-tidal carbon dioxide pressure.

[13]. Early recognition and proper treatment are important to improve the survival rate of patients with malignant hyperthermia. Although our patient showed a good clinical response to the discontinuation of the triggering agent and active cooling, the Malignant Hyperthermia Association of the United States recommends that all facilities where malignant hyperthermia-triggering anesthetics and depolarizing muscle relaxants are administered should stock dantrolene [14]. However, dantrolene is an expensive orphan drug and has a short lifespan; thus, dantrolene is still limitedly available and the routine preparation of dantrolene may not be possible in all hospitals [15]. Therefore, a systematic connection with other medical centers that have dantrolene in stock, or a national orphan drug center and rapid transfer system, would be very important. Here, we report a case of suspected malignant hyperthermia that was identified promptly and successfully managed intraoperatively. Intraoperative vigilance in the monitoring of vital signs cannot be overemphasized, and a prompt diagnosis with high suspicion is absolutely essential. We hope that this case report provides succinct and clinically applicable information on malignant hyperthermia and will help clinicians when they encounter similar cases.

NOTES

Conflict of interest
No potential conflict of interest relevant to this article was reported.

Ethical approval
The study was approved by the Institutional Review Board of Bundang Jesaeng Hospital (IRB No. 2021-03-009).

Patient consent
The patient provided written informed consent for the publication.

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