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## Suspected malignant hyperthermia during the 6<sup>th</sup> general anesthesia : A case report

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**Sirichotvithyakorn P. Suspected malignant hyperthermia during the 6<sup>th</sup> general anesthesia:  
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*The author reports a case of suspected malignant hyperthermia in a healthy 3-year-old girl with history of five uneventful anesthesia. The patient underwent re-implantation of the left ureter. After 80 min of general anesthesia with isoflurane, she developed hypermetabolic state (hyperthermia, hyperkalemia, and metabolic acidosis), elevated creatine phosphokinase and myoglobinemia, consistent with the diagnosis of malignant hyperthermia. The clinical grading scale of diagnosis of malignant hyperthermia was >50 (almost certain malignant hyperthermia). Isoflurane has been identified as the triggering agent. Treatment with dantrolene and supportive measures could make the patient survive the episode.*

**Keywords :** *Malignant hyperthermia, Complication, Adverse event, Isoflurane.*

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เด็กหญิงอายุ 3 ปีมาด้วยเรื่อง ภาวะไตบวมน้ำทั้ง 2 ข้างจาก vesicoureteric reflux ได้รับการให้ยาระงับความรู้สึกแบบทั่วตัว เพื่อผ่าตัด re-implantation ท่อไตข้างซ้าย isoflurane เป็นสารกระตุ้นให้เกิดภาวะ malignant hyperthermia โดยไม่มีการใช้สารกระตุ้นชนิดอื่น ผู้ป่วยเกิดภาวะหัวใจเต้นเร็วมาก อุณหภูมิขึ้นสูงถึง 40.9 องศาเซลเซียส ภาวะคาร์บอนไดออกไซด์ในเลือดคั่ง ความเป็นด่างมากกว่า -8 mEq/L ระดับ creatine phosphokinase ขึ้นสูง และพบ myoglobin ในเลือด การวินิจฉัยโดยใช้ clinical grading scale ได้มากกว่า 50 แต้ม (almost certain malignant hyperthermia) ได้ให้การรักษาโดยให้ dantrolene ทางหลอดเลือดดำ รวมทั้งการรักษาประคับประคองอื่น ๆ อาทิ การช่วยหายใจเพิ่มขึ้น เช็ดตัวด้วยน้ำเย็น การสวนล้างในช่องท้องและกระเพาะปัสสาวะด้วยน้ำเกลือเย็นจัด ผู้ป่วยอาการกลับเป็นปกติ และเฝ้าดูในโรงพยาบาล 7 วัน

**คำสำคัญ :** ภาวะ malignant hyperthermia, ภาวะแทรกซ้อน, Isoflurane.

Malignant hyperthermia is a rare, potentially lethal disorder of the skeletal muscle calcium homeostasis characterized by muscle contracture and life-threatening metabolic crisis following exposure to volatile anesthetics and depolarizing muscle relaxants. It was first described by Denborough and Lovell in 1960.<sup>(1)</sup> It has autosomal dominant inheritance with an incidence of approximately 1:150,000 in Thailand.<sup>(2)</sup> The author reports a case of suspected malignant hyperthermia in a 3-year-old girl with history of five uneventful anesthesia.

### Case Report

A well-developed, 3-year-old girl, 14 kg, ASA physical status I, was scheduled for re-implantation of the left ureter. Apart from that, she was healthy and had been anesthetized for genito-urinary tract surgery five times without any problem. The first four anesthetic records were not reviewed since the operation took place in other hospitals. Regarding the last anesthesia, she had received thiopental, atracurium, nitrous oxide, and isoflurane. Caudal bupivacaine and morphine was also performed for both intraoperative and postoperative analgesia. Her medical history was unremarkable. Her physical exam was within normal limits besides old surgical scars and uerterostomy opening on the left lower abdominal wall. The preoperative CBC, electrolytes, and urine analysis were normal. Her mother denied any drug allergies and there was no family history of adverse reactions involving neither anesthesia nor surgery.

No premedication was prescribed. An intravenous induction of anesthesia was carried out using thiopental 75 mg (5 mg/kg). Atracurium 8 mg (0.6 mg/kg) was given to facilitate endotracheal

intubation which was performed without any difficulty. Controlled ventilation was provided through a semiclosed CO<sub>2</sub> absorption circle; tidal volume 140-150 ml, respiratory rate 20 bpm, and peak inspiratory pressure 20 cmH<sub>2</sub>O. Anesthesia was maintained with isoflurane in nitrous oxide and oxygen (FiO<sub>2</sub> 0.5). Standard monitoring was used: electrocardiogram, noninvasive blood pressure, pulse oximeter, capnograph, and esophageal temperature. An induction of anesthesia was uneventful with heart rate of 120 bpm, SpO<sub>2</sub> 99-100 %, BP 90/40 mmHg, end-tidal CO<sub>2</sub> 38-40 mmHg, and BT 36.7 °C. Caudal block was performed using 0.25 % bupivacaine (without epinephrine) 10 ml (0.75 ml/kg) and preservative free morphine 0.7 mg (0.05 mg/kg). The patient was well draped and a water thermal blanket was placed underneath the patient to prevent hypothermia.

Anesthesia was uneventful for 80 min with a heart rate between 120 -130 bpm, temperature increased from 36.7 to 37.1 °C. The thermal blanket was then turned off. Ten minutes later, the temperature was 38.7 °C, heart rate increased to 150 -160 bpm, and end-expiratory CO<sub>2</sub> increased from 45 to 70 mmHg with a normal wave form and no inspired CO<sub>2</sub> on the gas analysis. A presumptive diagnosis of MH was made at this point. Isoflurane was discontinued. The patient was hyperventilated with oxygen 100 % using a fresh disposable non-rebreathing circuit. Anesthetic level was maintained with propofol and midazolam instead. A radial artery catheter was placed and blood sample was sent for arterial blood gas and biochemical analysis. Muscle rigidity was noted at patient's forearm during this procedure. Multiple cooling methods were attempted, such as external cooling with ice and water blanket, bladder and intraabdominal irrigation with

iced-cold saline by surgeons. Initial arterial blood gas analysis was returned shortly and revealed a combined respiratory and metabolic acidosis; pH 7.14, PaCO<sub>2</sub> 51 mmHg, PaO<sub>2</sub> 40.2 mmHg, HCO<sub>3</sub><sup>-</sup> 17.3 mEq/L, BE -10.7, Na 144 mEq/L, K 5.5 mEq/L. Sodium bicarbonate 15 mEq was administered to treat metabolic acidosis. More vigorous hyperventilation was attempted but hypercarbia could not be corrected. The tachycardia went up to 170 bpm and the temperature was rising rapidly to 40.9 °C. Injection of 28 mg of dantrolene (2 mg/kg), 50 min after the first symptoms were observed, improved the patient's situation within 10 min – heart rate 130 bpm, arterial blood pressure 110/70 mmHg, body temperature 40 °C. End-expiratory CO<sub>2</sub> gradually decreased and was back to normal 15 min later. Another arterial blood gas analysis after dantrolene treatment was as follow; pH 7.2, PaCO<sub>2</sub> 38 mmHg, PaO<sub>2</sub> 296 mmHg, HCO<sub>3</sub><sup>-</sup> 17.4 mEq/L, BE -3.8, K 7.28 mEq/L. One more dose of sodium bicarbonate was administered. Forced diuresis was induced with furosemide.

The temperature returned to 38 °C 60 min after dantrolene injection and cooling was discontinued. The operation was concluded by this time. Repeated arterial blood gas showed pH 7.25, PaCO<sub>2</sub> 45 mmHg, PaO<sub>2</sub> 432 mmHg, HCO<sub>3</sub><sup>-</sup> 19.8 mEq/L, BE -7.1, K 4.1 mEq/L, and Na 140 mEq/L. The patient was then transferred to the pediatric intensive care unit (PICU).

At the PICU, the patient was continuously monitored on temperature and end-expiratory CO<sub>2</sub>. Dantrolene was continued at 1mg/kg every 6 hours for 24 hours. The child was also given sodium bicarbonate infusion in order to maintain alkalinized urine to facilitate myoglobin excretion. Laboratory studies taken during surgery showed hyperkalemia

5.9 mEq/L, serum myoglobin 0.106 mg/dl and creatine phosphokinase level 427 IU/L. Coagulation profiles were normal. Urine heme was 3+. On the following day arterial blood gas was normal; pH 7.51, PaO<sub>2</sub> 104mmHg, PaCo<sub>2</sub> 31.6 mmHg, HCO<sub>3</sub><sup>-</sup> 24.8, and BE 1.8. There was no further sign of MH. The patient was observed in PICU for 24 hours then transferred to an ordinary pediatric ward and subsequently discharged 7 days after operation. The patient's family was informed and counseled but the diagnostic test was denied.

## Discussion

Malignant hyperthermia is an inherited hypermetabolic disorder of the skeletal muscle triggered by depolarizing muscle relaxants and potent inhalation anesthetic agents. The incidence has been reported as 1:50,000 anesthetics administered in adults and 1:15,000 in children.<sup>(3-4)</sup> In Thailand, the first MH case was reported in 1979<sup>(5)</sup> followed by other cases reported from many regions of the country.<sup>(2,6-8)</sup> The approximated incidence of suspected MH by the Thai Anesthesia Incidents Study (THAI study) was 1:150,000.<sup>(2)</sup>

MH is potentially fatal if undetected. The clinical signs are not uniform and the onset varies. As in this case, neither family history nor previous exposure to anesthesia reliably predicts MH occurrence. Strazis et al studied 503 suspected cases of MH and found that 20.9 % had previously uneventful anesthesia and 75.9 % were absent of positive family history.<sup>(9)</sup> Some cases were reported regarding MH crisis following uneventful anesthesia. Striebel et al<sup>(10)</sup> described an MH crisis during the 6<sup>th</sup> general anesthesia using isoflurane in a 30-year old

female who had been anesthetized repeatedly without complications. Some patients endured anesthesia using isoflurane with or without succinylcholine but developed MH crisis during desflurane administration later.<sup>(11-12)</sup> Claxton et al<sup>(13)</sup> reported a case of previously investigated malignant hyperthermia-susceptible patient who did not declare his status and was exposed to both succinylcholine and isoflurane, without any reaction. Our patient underwent 2 general anesthesia within one year in our institute, using the same triggering agent, isoflurane. She did not develop MH in the first place but in the last one.

The most frequent and earliest sign of MH crisis is unexplained, unexpected tachycardia together with unexplained, unexpected rise end-expiratory CO<sub>2</sub>, which corresponded with this case. The other clinical presentation includes hyperthermia, muscle rigidity, metabolic acidosis and rhabdomyolysis. Other conditions that may resemble the MH situation include- but not limited to- iatrogenic overheating, thyroid storm, heat illness, pheochromocytoma, sepsis, and neuroleptic malignant syndrome.

The patient received no other trigger agents but isoflurane. When the trigger is thought to be one of the inhalational agents, the onset is usually more insidious and may take hours, whereas when it develops after the administration of depolarizing muscle relaxant, the onset occurs within minutes.

Upon establishing the diagnosis, immediately discontinue the triggering agents and administer 100 % oxygen. Call for additional experienced help. Hyperventilate at two to three times the predicted minute ventilation. Administer 2.5 mg/kg dantrolene intravenously and repeat as often as necessary titrated

to control clinical signs of MH. Dantrolene should be continued for at least 24 hours after control of the episode (approximately 1 mg/kg every 6 hours). Other supportive measures, such as cooling, treatment of hyperkalemia and metabolic acidosis, should be promptly initiated.<sup>(14)</sup>

The most widely used and most sensitive method that determines whether an individual is susceptible to MH is caffeine-halothane contracture test (CHCT), which is the gold standard. Since the test is only available in some medical centers in North America and Europe, as well as the patient's parents refused to have a muscle biopsy test, we have graded the patient's clinical findings according to a clinical grading scale<sup>(15)</sup> and found the likelihood of MH as "almost certain" (>50 points-(a) generalized muscle rigidity, (b) K>6mEq/L, myoglobin, raised CK, (c) inappropriate hypercarbia, (d) inappropriate rapid increase in temperature, (e) inappropriate sinus tachycardia, and (d) response to dantrolene/metabolic acidosis).

The patient was observed in an ICU for 24 hours as recommended by the Malignant Hyperthermia Association of United States (MHAUS) since the recrudescence occurs in about 25 % of MH cases.<sup>(14)</sup>

In conclusion, the author hereby reports a rare case of suspected malignant hyperthermia in a 3-year-old girl who completely recovered after dantrolene and supportive treatment. It should be emphasized that history of a past uneventful anesthesia cannot reliably predict the occurrence of malignant hyperthermia. Therefore, properly monitoring and handy availability of dantrolene are essential to lowering the mortality of MH.

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