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# A rare complication of anesthesia in newborn: malignant hyperthermia

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***Summary***

Malign hyperthermia is a rare anesthesia-related disorder which may be fatal. Here, we present a newborn who developed malign hyperthermia after general anesthesia and recovered with dantrolene treatment. Anesthesia with sevoflurane was performed in the patient planning examination of the upper airways under general anesthesia. One hour after anesthesia the patient developed hyperthermia, tachycardia, tachipnea and muscle rigidity and a diagnosis of malignant hyperthermia was made with clinical and laboratory findings. The findings improved dramatically with dantrolene treatment. *(Turk Arch Ped 2012; 47: 208-210)*

**Key words:** Anesthesia, malignant hyperthermia, newborn

## Introduction

Malignant hyperthermia is a hypermetabolic response which occurs against inhalation agents, muscle relaxants and rarely against stress conditions including excessive exercise and heat. The incidence of this genetic hypersensitivity which may be life-threatening has been reported to be 1 in 50000 anesthetics in adults and 1 in 15000 anesthetics in children. It is observed with a 2 fold higher frequency in boys compared to girls (1).

The diagnosis of malignant hyperthermia is based on clinical findings or laboratory tests. Clinical findings include hyperthermia, unexplained increase in pCO2 (partial pressure of carbon dioxide), muscle rigidity, tachycardia, acidosis and hyperkalemia. The gold standard for diagnosis is in-vitro contracture test (IVCT). In genetic tests, mutations in the "ryanodine" receptor-1 (RYR1) gene on the 19th chromosome were shown to be associated with MH. In treatment, discontinuation of the triggering agent, supportive approaches and dantrolene which is the only know specific drug are used (1,2,3,4,5).

Here, a newborn who developed MH after general anesthesia and improved with dantrolene treament has been presented.

## Case

Positive pressure ventilation was performed in the delivery room in the newborn who was born by cesarean section with 6/8 APGAR score with a birth weigth of 4050 g at the 39th gestational week from nonconsanguineous parents. Afterwards the newborn was internalized in the neonatal unit with a prediagnosis of respiratory distress and choanal atresia. Examination in terms of choanal atresia and upper respiratory tract obstruction under general anesthesia was planned. Only inhaled sevoflurane was given as anesthetic substance and a body temperature of 38.8°C was found one hour after anesthesia. During the follow-up, the body temperature reached 42°C in minutes and tachypnea, tachycardia and muscle rigidity developed in addition. Respiratory arrest developed and the patient was intubated. The patient whose blood gases revealed a pH value of 7.24 and a $pCO_2$ value of 65 mmHg (respiratory acidosis, hypercapnia) was connected to mechanical ventilator. Laboratory tests revealed a serum potasium value of 6.3 mmol/L and a creatinine kinase (CK) value of 414 U/L (N:38-174 U/L). Coagulation tests were found to be normal. In addition to supportive treatments dantrolene at a loading dose of 2,5 mg/kg was given intraveneously to the patient in whom MH was considered with clinical and laboratory findings according to the scoring system developed by Larach et al. (2). Within two hours after dantrolene treatment the body temperature of the patient reduced to 36.4°C and muscle rigidity improved. The need for respiratory support decreased and the patient was separated from the mechanical ventilator by performing extubation in 12 hours. Dantrolene treatment was continued at a dose of 1 mg/kg for 48 hours. In the laboratory follow-up, CK level increased up

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to 16185 U/L, hyperpotassemia improved and disseminated intravascular coagulation (DIC) did not develop. It was learned that no similar history was present in the family of the patient. IVCT was not performed in the baby who was considered to have MH with clinical findings, laboratory tests and the response to dantrolene treatment because he was very young. Genetic analysis for RYR1 mutation could not be performed, since the family did not give consent. Currently the patient is 19 months old and is growing up without problem. The family members were informed about MH.

## Discussion

MH which is triggered by anesthetic substances is a rare complication related to anesthesia which may be fatal. All inhaled anesthetics except for nitric oxide and succinyl choline which is a muscle relaxant may lead to MH. Malignant hyperthermia crisis may develop during the first exposure to anesthesia. Sometimes, the crisis can be triggered even after the third anesthesia. It may develop at any time during anesthesia and during the early post-operative period (1,3,6). In our patient, the findings developed in the first hour after the first anesthesia with sevoflurane which is an inhaled anesthetic.

The earliest clinical findings include tachycardia, tachypnea and increased $pCO_2$ in association with rapid increase in body temperature. When hyperthermia develops, the body temperature increases by 1-2°C every 5 minutes. When exposure to anesthetics occurs, intracellular calcium (Ca+2) increases in striated muscles and myofibril contraction and muscle rigidity develop as a result of excessive Ca+2 discharge into the cytoplasma. Uncontrolled hypermetabolism causes cellular hypoxia and gradually worsening metabolic acidosis. If untreated, rhabdomyolysis which develops with myocyte necrosis results in life-threatening hyperkalemia. Myoglubinuria causes acute renal failure. Other complications include heart failure, intestinal ischemia and compartment syndrome. Maintenance of the body temperature may lead to organ dysfunction and development of DIC may lead to death (1,7). The first finding in our patient was hyperthermia (the body temperature increased to 42°C in minutes). With following muscle rigidity, tachycardia, tachypnea and accumulation of $pCO_2$ the patient was connected to the ventilator. Myoglubinuria and DIC did not develop in our patient who had hyperkalemia.

The accepted diagnostic test to determine predisposition to malignant hyperthermia is IVCT. This test is based on evaluation of contraction response by exposing a muscle sample obtained

**Table 1. The scoring system used in the diagnosis of malignant hyperthermia (2)**

| Findings | Symptoms | Score |
|---|---|---|
| **Muscle rigidity** | Diffuse muscle rigidity | 15 |
| | Severe massater muscle rigidity | 15 |
| **Muscle destruction** | Serum CK level >20 000 IU, (after anesthesia which includes succinyl choline) | 15 |
| | Serum CK level >10 000 IU, (after anesthesia which does not include succinyl choline) | 15 |
| | Dark urine during surgery | 10 |
| | Increase in urinary myoglobin level | 5 |
| | Increase in serum myoglobin level | 5 |
| | Blood/plasma/serum potassium >6 mEq/L | 3 |
| **Respiratory acidosis** | $PCO_2$>55 mmHg with appropriate controlled ventilation | 15 |
| | $PaCO_2$>60 mmHg with appropriate controlled ventilation | 15 |
| | $PCO_2$>60 mmHg with spontaneous ventilation | 15 |
| | $PaCO_2$>65 mmHg with spontaneous ventilation | 15 |
| | Hyperkapnia | 15 |
| | Tachypnea | 10 |
| **Increase in body temperature** | Rapid increase in body temperature | 15 |
| | A body temperature of >38.8 ºC | 10 |
| **Cardiac involvement** | Unexplained sinus tachycardia | 3 |
| | Ventricular tachycardia or ventrcular fibrilation | 3 |
| **Familial history** | History of MH in first-degree relatives | 15 |
| | History of MH in non-first-degree relatives | 5 |
| **Other** | Base excess in blood gases >-8 m/Eql | 10 |
| | pH <7.25 in blood gases | 10 |
| | Rapid improvement in metabolic and/or respiratory acidosis findings with dantrolene | 5 |
| | Presence of another criterion with familial history (other than high CK at rest) | 10 |
| | High CK level at rest (in the patient with a familial history of MH) | 10 |

| Table 2. Evaluation of scoring (2) | | |
|---|---|---|
| **Score range** | **MH degree** | **Definition of propabililty** |
| 0 | 1 | Not probable |
| 3-9 | 2 | Very low probability |
| 10-19 | 3 | Low propability |
| 20-34 | 4 | Probable |
| 35-49 | 5 | Possible |
| >50 | 6 | Definite |

MH: malignant hyperthermia

with open muscle biopsy to special test substances (including halotane and caffeine) at increasing doses in vitro. This test was standardized by "Europe Malignant Hyperthermia Group" and reported to have a sensitivity of 99% and a specificity of 93.6%. The test is not widely used because of difficulty of biopsy especially in babies and and because of its high cost (4,8,9). When this test can not be performed, the diagnosis can be made with the scoring system developed by Larach et al. (2) (Table 1 and 2). According to this scoring system our patient received a total score of 73 [(I) diffuse muscle rigidity (15 points), (II) CK>10 000 IU with anesthesia which did not include succinyl choline (15 points), (III) $PaCO_2$>60 mmHg with spontaneous ventilation (15 points), (IV) rapid increase in body temperature (15 points), (V) unexplained sinus tachycardia (3 points), (VI) blood gases pH<7.25 (10 points)] and found to be compatible with "sixth degree" and "definite" MH. In addition, response to dantrolene treatment supported the diagnosis.

The Ca+2-release channel of sarcoplasmic reticulum (SR) is the ryanodine receptor. Genetic studies have shown that autosomal mutations are present in RYR1 gene in subjects with a clinical picture of MH. These mutations lead to uncontrolled increase in oxidative metabolism in the skeletal muscle with excessive Ca+2 release into the cell, excessive oxygen consumption and production of $pCO_2$. The superiority of genetic testing to IVCT is the fact that it is noninvasive, has a lower cost and does not have disadvantages related to muscle biopsy (10,11,12). Genetic analysis could not be done in our patient, since the family did not give consent.

Treatment of malignant hyperthermia includes discontinuation of the predicted triggering drug or condition, oxygenation, improvement of acidosis and electrolyte abnormalities, mechanical cooling and administration of dantrolene. Cooling of the body temperature up to 38.5°C using cooling methods is recommended for hyperthermia. The coagulation profile should be checked every 6-12 hours. Specific medical treatment of MH which can be fatal if untreated is dantrolene (1,11). In our patient, recovery of clinical and laboratory findings which developed after anesthesia with dantrolene treatment supported the diagnosis.

In Europe and North America, MH was the most common reason of death related directly to general anesthesia in 1970s and the mortality rate was reported to be 70-80%. Currently, the mortality rate has decreased to below 10% with recognition of the condition, diagnostic advances and use of dantrolene in treatment (12).

MH can develop unexpectedly during surgical anesthesia and after anesthesia. It is important for physicians to make the diagnosis rapidly and start dantrolene treatment immediately in this condition which may be fatal. Rapid diagnosis and urgent intervention in this condition which is observed very rarely in the newborn period is life-saving. In addition, informing family members is important because of genetic predisposition.

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