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Management of Malignant Hyperthermia (MH)

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Abstract

Malignant hyperthermia is a potentially fatal genetic defect characterized by disturbance of calcium level in skeletal muscle. Volatile anesthetics and/or the depolarizing muscle relaxant succinylcholine may trigger this hyper-metabolic muscular syndrome due to uncontrolled sarcoplasmic Ca release via functionally altered Ca release receptors, leading to tachycardia, muscular rigidity, hypoxemia, hypercapnia, acidosis, hyperkalemia, and hyperthermia in susceptible individuals.

Survival of affected patients depends crucially on the early recognition of symptoms, and characteristic of MH, and immediate action on the part of the presenting anesthesiologist. Since the clinical presentation of malignant hyperthermia is highly variable, the present study includes 3 cases of MH and highlights the timely identification of symptoms for rescuing the patient.

In the first case the patient did not survive due to the late noticing of the disorder, for the second case, the patient was treated and managed. lastly, the third case the treatment was unavailable therefore the patient could not be managed. Clinical symptoms of malignant hyperthermia, and current therapeutic guidelines, as well as adequate management of anesthesia in patients susceptible to malignant hyperthermia, are discussed in this report.

Introduction

Malignant hyperthermia (MH) is a rare, but life-threatening disorder, it is inherited in an autosomal dominant pattern. A potentially lethal hypermetabolic syndrome that may lead to metabolic crisis of skeletal muscle in susceptible individuals following exposure to triggering agents such as volatile anesthetics agents (halothane, enflurane, isoflurane, sevoflurane, and desflurane) or depolarizing muscle relaxants such as suxamethonium[(1)].

in the course of excitation–contraction coupling, acetylcholine evokes an action ability on the neuromuscular endplate. This action potential is propagated to the transverse tubule, inflicting displacement of the rate on the dihydropyridine receptor. A conformational change on the voltage-gated dihydropyridine receptor is directly transmitted to the ryanodine receptor subtype 1 (RYR1) at the sarcoplasmic reticulum, which responds by opening a big ion channel, allows launch of calcium from the sarcoplasmic reticulum into the cytosol, leading to muscle contraction by initiating cross-linking of myofilaments [(1)].

active reuptake of calcium into the sarcoplasmic reticulum via an adenosine triphosphate-dependent calcium pump terminates the muscle contraction. In an MH crisis, the triggering agent induces extended opening of functionally altered ryanodine receptors, resulting in uncontrolled release of calcium from the sarcoplasmic reticulum and ongoing muscle activation presenting as rigidity [(1)].

additionally, consistent activation of aerobic and anaerobic metabolism results in expanded oxygen intake, leading to hypoxia, progressive lactic acidosis, excessive production of CO2, and increased body temperature. Calcium reuptake into the sarcoplasmic reticulum and sustained muscle contraction consume large amounts of adenosine triphosphate. Depletion of cellular adenosine triphosphate stores results in protracted muscular rigidity and ultimately to rhabdomyolysis, finally, breakdown of membrane integrity results in release of the contents of cells (eg, potassium, creatine phosphokinase, myoglobin) into the circulation [(1)].

The overall incidence of MH is estimated to be between 1 in 5000 and 1 in 200000 anesthetic procedures. The prevalence of MH susceptibility could be as high as 1 in

3000 in the general population. Because of the widespread use of volatile anesthetics during different types of surgeries, MH remains a relevant concern [(2)].

MH is still a relevant complication and every anesthesiologist must recognize the symptoms of an MH episode and start appropriate treatment without delay. MH may occur at any time in the course of anesthesia as well as in the early postoperative duration, but not after an hour of discontinuation of risky agents. The earliest signs are tachycardia, rise in end-tidal carbon dioxide concentration regardless of increased minute volume, followed by muscle rigidity, in particular following succinylcholine administration [(3)] .

body temperature elevation can be a dramatic sign of MH. Hyperthermia can be marked, with an increase in core temperature by 1–2 °C each five minutes. severe hyperthermia (core temperature more than 44°C may additionally arise, and result in a marked increase in oxygen intake, CO2 production, widespread critical organ dysfunction, and disseminated intravascular coagulation (DIC) [(1)].

The prognosis of an MH crisis depends on how soon MH is suspected and how rapidly appropriate treatment is initiated. Administration of trigger agents must be stopped immediately and anesthesia should be continued using intravenous opioids, sedatives, and, if necessary, nondepolarizing muscle relaxants. Treatment includes immediate administration of dantrolene 2 mg/kg, which should be repeated every 5 minutes until the cardiac and respiratory systems are stabilized [(1)].

Dantrolene, a hydantoin derivative, acts as a specific ryanodine receptor antagonist and inhibits release of calcium from the sarcoplasmic reticulum without improving its reuptake. Specific side effects are rare, but include prolonged breathing problems, tissue necrosis after accidental extravasation, nausea, vomiting, headache, and dizziness. Patients experiencing MH should receive dantrolene and be monitored closely for 48–72 h, since (even despite dantrolene treatment) 25 % of patients will experience a recurrence of the syndrome [(1)].

Tests for disseminated intravascular coagulation (DIC) should be included as well as observation of urine for myoglobinuric renal failure. DIC is most frequent when body temperature exceeds about 41 ° C. Since masseter muscle rigidity (MMR) may presage MH, it is most advisable to discontinue the trigger anesthetic after MMR. In an emergency, the anesthesia may continue with “non-trigger” drugs. Following MMR, patients should be admitted to an intensive care unit and monitored for signs of MH [(1)].

Rhabdomyolysis occurs in virtually all patients experiencing MMR and the creatine kinase (CK) values should be checked regularly. Dantrolene should be administered if the other signs of MH occur along with MMR. Muscle biopsy for definitive diagnosis should be carefully considered. It is remarkable that dantrolene may be efficacious in treating hyperthermia from many causes unrelated to MH with anesthesia. Based on the similarity between a variety of drug induced hyperthermic syndromes and MH, dantrolene has been used effectively to treat several other syndromes such as the neuroleptic malignant syndrome, MDMA toxicity and hyperthermia related to new onset of juvenile diabetes in adolescents [(1)] .

Materials and methods

Searching the internet for cases of malignant hyperthermia, an article titled clinical treatment of malignant hyperthermia in three cases in PubMed written by, Tao Pan, Wenli Ji, Mengqi Nie, Yang Li

Other articles titled management of malignant hyperthermia was published in Pubed by Daniel Schneiderbanger, Stephan Johannsen, Norbert Roewer, and Frank Schuster.

As well as a review in Biomed journal written by Henry Rosenberg, Neil Pollock, Anja Schiemann, Terasa Bulger & Kathryn Stowell. Mendely used for citation and bibliography

Case report I

The patient was a male aged 7 years and had a body weight of 28 kg. He was admitted to hospital on July 9, 2000 for hernial repair. Preoperative blood routine examination was normal. Only 30 min before surgery, 30 mg luminal and 0.2 mg atropine was injected intramuscularly, and 50 mg ketamine and 3 mg midazolam for anesthesia was injected intravenously.

However, due to poor anesthetic effect, ketamine was added twice, each time 100 mg. The surgery lasted 30 min and the child in surgery displayed stable vital signs, with a total capacity of ketamine 250 mg. The child was unconscious after the operation [(4)].

Case report II

The patient was a male aged 12 years. He was admitted to hospital on July 8, 2010 for hernial repair. On admission, surgery done under continuous epidural anesthesia. Half an hour before surgery, 50 mg luminal and 0.5 mg atropine was injected intramuscularly, the child was given 5 ml 0.894% ropivacaine and 2% lidocaine mixture, no abnormality was observed within 5 min, the ropivacaine were given in fractions with a total of 10 ml[(4)].

Case report III

57 years male patient. admitted to the hospital due to paraplegia caused by abdominal trauma before 4 hours. His physical examination at the admission showed a body temperature of 37°C, P 88 per/min, R 22 per/min, BP 105/80 mmHg.The patient was conscious and his neck was soft, chest clear, no wet and dry rales were heard. abdomen was soft, no tenderness, no rebound tenderness [(4)].

Results

In case I, the child went through convulsions, high fever and succumbed within a few hours. High fever was not detected in a timely manner, which is one of the main symptoms of MH therefore the management was a failure.

At 1:40 p.m., convulsions and high fever occurred, and his body temperature reached 40.2°C. Physical cooling and antipyretic drugs showed poor results.

At 5:00 p.m., he was transferred into the ICU. the child suffered persistent high fever and his heart rate was 140–160 per/min, breathing 40–45 per/min, blood pressure 82/40 mmHg, oxygen saturation fluctuated between 80–84%, skin temperature was low, the skin circulation was poor, and there was abundant bloody sputum in the airway.

At 4:00 a.m. of July 13, the child's heart rate, blood pressure decreased significantly (heart rate 38 times/min, blood pressure 20/10 mmHg), epinephrine was immediately injected intravenously and intermittently, along with sustained chest compressions, but the result was ineffective and the child was declared clinically dead at 4:35 a.m.

In the second case, a 12-year-old male child had convulsions and high fever after simple surgery caused by MH. Once confirmed, immediate measures were taken to lower the body temperature and the child was rescued. The surgery lasted for 1.5 h and anesthesia lasted for 3 h. After the operation, the child suffered convulsions, high fever, and his body temperature reached 40.7°C. After being transferred to ICU, the child suffered persistent high fever, his heart rate stayed at 170 times/min, breathing was 51 times/min, blood pressure 90/57 mmHg, oxygen saturation fluctuated at around 50%.

He was unconscious with cold extremities, breathing was normal. But with tachycardia. After admission to ICU, it was supposed that the child's high fever was caused by lidocaine-induced malignant hyperthermia (MH), thus immediate measures were taken to lower his temperature. After few days form ICU admission and appropriate management, the child then transferred back with mild neuropsychiatric symptoms. And finally, was discharged home.

In the last case, a male 57-year-old was admitted to hospital due to paraplegia. The patient underwent more critical conditions once symptoms of MH appeared. power in the upper limbs was grade 4, muscle strength of lower limbs was zero grade, muscle tone was normal, loss of sensation of the lower extremities, the patient revealed abdominal pain and discomfort, abdominal puncture showed non-condensable blood, ultrasound abdomen showed large amount of fluid in abdominal cavity.

Urgent laparotomy was conducted, there was extensive contusions observed in the stomach, duodenum, transverse colon and pancreas and lacerations in transverse mesocolon, gastroepiploic, retroperitoneal hematoma, intra-abdominal Repair surgery on gastroepiploic and transverse mesocolon was conducted and the patient was transferred into ICU after the surgery.

In the operation, propofol and vecuronium were injected intravenously for anesthesia instead of using inhaled anesthetics. ECG showed high edge of T wave, the IV injection of high glucose, calcium and continuous intravenous infusion of sodium bicarbonate showed poor results.

ECG monitoring showed that the patient's heart rate gradually slowed down to 60–80 per/min, the IV injection of high glucose, calcium and continuous intravenous infusion After being hospitalized for 4 h, the patient's temperature rose to 38.6°C, which increased further after 9 h to 39. 6°C.

his muscle was stiff, then the patient suffered ventricular fibrillation, immediate cardiac compressions, defibrillation and intermittent intravenous injection of epinephrine were given to him. Later, the patient presented with ventricular fibrillation that then converted to sinus rhythm. Review of chest with ultrasound showed no pleural effusion or pericardial effusion, but a little peritoneal effusion and subcapsular fluid under the left kidney.

due to critical condition, the patient's family signed away the rescue and the patient was automatically discharged

Discussion

Some patients with congenital diseases such as idiopathic scoliosis, strabismus, ptosis, umbilical hernia, inguinal hernia and other diseases are prone to MH during anesthesia. At present, the gold standard for the diagnosis of MH is caffeine halothane skeletal muscle contraction experiment, where the muscle biopsy should be taken under local anesthesia. When the caffeine halothane skeletal muscle contraction experiment is not practical, we can assess clinical indicators of the MH to help us understand the possibility of MH. If the score is over fifty points, the identification is nearly sure. For MH management, the main approach is to instantly stop the triggering agent, and start efforts to lower the body temperature and start intensive supportive therapy for the affected organs. In case 1, the child underwent really easy surgery when indefinite quantity of ketamine was 250 mg. The child's convulsions and high fever were purported to be caused by MH. In fact, an excessive dose of ketamine has been given.MH score for him reached 53 points and identification of it absolutely was nearly sure. In case 2, the patient's convulsions and high fever were also supposed to be caused by MH. The patient also had a history of the use of lidocaine with no symptoms of

infection and no infusion reactions. His MH score was 53 points and diagnosis of MH was almost certain. In case 3, the patient was admitted to hospital due to paraplegia, when entering into ICU, his muscular tension of both lower limbs was high and his muscle was stiff and rigid, which could not be explained by spinal cord injury. The patient had no history nor signs of head trauma and he was conscious. Possibility of traumatic brain injury was excluded to cause an increase in his muscle tension of both lower limbs, its rigidity and its tightness, the main region of the patient's trauma was in the abdomen and not the lower limbs, rhabdomyolysis could not be explained by muscle trauma although the patient had no family history of MH. Inhalation anesthetic, ketamine, lidocaine were not used in the operation, postoperative body temperature rose slowly, the total score of MH of the patient reached up to 65 points and patients clinical manifestations could only be explained by MH. High fever had not been detected timely in the treatment of the first case of MH, unfortunately due to insufficient knowledge of the disease. The symptomatic treatment of high fever was not sufficient, leading to death of the child caused by rapid multi organ failure. All measures were taken to cool his temperature (physical cooling, antipyretic medication, internal cooling by using cold saline through a nasogastric tube, as well as a cold enema infused rectally, intravenous infusion of cold fluids at 4°C has been given in effort to lower the core body temperature). In the treatment of the first and third case, special effect antidote dantrolene was unavailable, so the course of the disease could not be blocked although active symptomatic treatment has been done, the patient still died and In case 2, after the onset of the disease, antidote dantrolene was given at once. The child's condition was significantly alleviated after oral administration of dantrolene. Active cooling and application of special effect antidote dantrolene played a key role in the successful treatment of the child. The active management of cooling and using of dantrolene in addition to using renal replacement therapy(CRRT) helped significantly to improve the patient condition and his survival. The initial clinical manifestations of case 3 were not typical, DIC progressed rapidly, and the disease ended up into a MOF stage shortly thus losing the opportunity for treatment, lead to loss of patient [(4)].

Conclusion:

The management of MH crucially depends on the understanding of the pathophysiology of disorder and its clinical manifestation as bad timing of initiation of treatment can lead to death.

Reference

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