Perioperative Considerations for Suspected Malignant Hyperthermia

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Malignant hyperthermia (MH) is a life-threatening disease which could be fatal. Volatile agents and suxamethonium are the leading causes of the abrupt rise of temperature and muscle contraction.

The anesthesiologist must be aware of the pathophysiology of malignant hyperthermia and the techniques to avoid the occurrence of this complication.

A sixty-three-year-old female with a family history of malignant hyperthermia, who underwent axillary lymph node biopsy; the techniques to avoid the precipitation of malignant hyperthermia were used.

Malignant hyperthermia (MH) is an autosomal dominant and hypermetabolic condition which could lead to an increase in the end tidal carbon dioxide level, tachycardia, muscle rigidity, hyperpyrexia and an increase in oxygen consumption after exposure to potent volatile anesthetic agents such as sevoflurane, desflurane, isoflurane, halothane, and depolarizing muscle relaxants like succinylcholine. An early sign of MH is hypercapnia despite an increase in minute ventilation. Survival from malignant hyperthermia is highly dependent on early recognition and aggressive treatment. The pathophysiology of MH involves an excessive production of calcium from the sarcoplasmic reticulum which could lead to muscle activation, and thus contraction occurs. Confirmation of the diagnosis can be done by DNA sequencing technology and in vitro contracture testing, which is rarely done due to its costs.

The aim of this case report is to increase awareness regarding the prevention of malignant hyperthermia among anesthesiologists, especially in susceptible patients.

THE CASE

A sixty-three-year-old female, known case of osteoporosis, breast cancer and a family history of malignant hyperthermia, was scheduled for elective surgery for left axillary sentinel lymph node biopsy. She was diagnosed with grade 1 bilateral invasive ductal carcinoma. Family history revealed that her brother died forty years ago, most likely due to malignant hyperthermia. She had a history of lumpectomy, which was performed under general anesthesia without any complications. On physical examination, she weighed 56 kg and a height of 154 cm. Neurological, respiratory and cardiac exams were unremarkable. Laboratory investigations were within normal range. Due to a positive family history of malignant hyperthermia, necessary precautions were taken before her arrival to the operation theatre. All inhalation agents were removed from the operation theatre. A new breathing circuit as well as soda lime (carbon dioxide absorbent) were inserted. The circuit was flushed overnight with Oxygen. After eight hours of fasting, the patient was attached to non-invasive blood pressure monitoring, pulse oximetry, and electrocardiogram. Precautions were taken for both upper arms due to previous bilateral lumpectomy. Therefore, intravenous line gauge was inserted on the right leg and induction was done with propofol

1.5mg/kg, fentanyl 2mcg/kg, lidocaine 1mg/kg, cisatracurium 0.1mg/kg and midazolam 3mg. Laryngeal mask airway was inserted. Maintenance of anesthesia was done via 50 percent of oxygen and 50 percent of air. Total intravenous anesthesia was achieved using propofol 60-70cg/kg/min and remifentanil 0.02-0.03 mcg/kg/min. Despite the lack of bispectral index (BIS) monitor, the patient's vital signs were closely monitored. Almost fifteen minutes before the surgery ended, propofol and remifentanil were tapered off. Ringers lactate was used to maintain hemodynamics. At the end of the surgery, the patient received ondansetron 4mg, paracetamol 1g and diclofenac 75mg. The patient had stable hemodynamics throughout the one-hour of surgical procedure. The patient was fully awake during extubation and then transferred to the recovery room. Her hospital stay was uneventful.

DISCUSSION

Malignant hyperthermia is an autosomal dominant condition which could be elicited by exposure anesthetic volatile agents and succinylcholine with exception to nitrous oxide[1]. MH is a hypermetabolic state, which could rarely happen without being exposed to anesthetic medications. However, exercise and heat-stroke are considered to be potential triggers for MH crisis[2]. It is estimated that the incidence of malignant hyperthermia is 1:10000[3]. MH can occur in males and females without gender preference and at any age. The evidence suggests that MH crisis can develop with the first exposure, however, an average of three exposures to anesthesia are required to have such crisis[4]. Also, it has been found that other creatures can develop MH like pigs, horses and dogs[5]. The differential diagnoses of malignant hyperthermia include sepsis, thyroid storm, pheochromocytoma, iatrogenic overheating, neuroleptic malignant syndrome (NMS), serotonin syndrome and 3,4-methylenedioxymethamphetamine (MDMA) overdose[1]. The clinical diagnosis of MH crisis largely depends on the recognition of the early signs which include tachycardia, increase end-tidal carbon dioxide, which is considered to be the most sensitive sign despite hyperventilation, and muscle rigidity[6]. The core temperature can increase by a rate of 1-2c every 5 minutes. Hyperthermia could cause an increase in oxygen consumption, CO2 production and vital organ dysfunction[7]. The pathophysiology of MH involves the presence of a defect in the Ca channel, which is located in the

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skeletal muscle sarcoplasmic reticulum. The channel is called ryanodine receptor 1 (RyR1) located on chromosome 19q13.1, and accounts for 70% of the genes responsible for causing MH in susceptible families[8]. This channel is associated with other protein receptors that have a potential or known role in RyR1, such as dihydropyridine receptor, SR membrane proteins (SRP-27 junctate), transient receptor potential cation channel (TRPC) family and plasma membrane-associated proteins (eg. CIC-1 chloride channels and Na^+/Ca^{2+} exchangers). After exposure to the trigger, the receptors get activated and lead to uncontrollable Ca release from sarcoplasmic reticulum[1].

King or King-Denborough syndrome (KDS) is congenital hypotonia, characterized by a minor delay in motor development, and is associated with malignant hyperthermia[9]. Other syndromes such as Central Core Disease (CCD), Myotonic Muscular Dystrophy (MMD) and centronuclear myopathy were found to be associated with MH[1]. Studies suggest that 50% of patients experiencing succinylcholine-induced masseter muscle rigidity (MMR) are susceptible to MH[10]. The diagnosis can be confirmed clinically by the signs and symptoms as well as laboratory testing. Two laboratory tests are used for diagnosis, in vitro contracture test and DNA analysis. The former is based on the contraction of muscle fiber after exposure to halothane or caffeine. The European Malignant Hyperthermia Group (EMHG) consider a patient as being susceptible to MH (MHS) when both caffeine and halothane tests are positive. An individual can also be diagnosed when either test are positive (halothane or caffeine), and these individuals are designated as MHS(h) or MHS(c)[11]. Dantrolene is the treatment of choice of MH which acts by inhibiting the DHPR in a RyR1 and reducing their activity. Dantrolene was first introduced in 1979 and has been shown to decrease the mortality rate from 80% to 1.4%[12]. The treatment of an acute MH crisis includes the immediate discontinuation of triggering agents, hyperventilation, administration of dantrolene in doses of 2.5 mg/kg repeated until MH subsides, cooling by all routes available (intravenous saline at 4° C, topical ice to all exposed areas, peritoneal exchange), urine catheter should be inserted to maintain urine output 2ml/kg/hour, extraction blood gases, electrolytes, creatine kinase, blood and urine for myoglobin and treat hyperkalemia and arrhythmia as needed. Continue Dantrolene as 1 mg/kg every 4–8 h for 24–48 h, monitor the patient in high dependency unit for 24 hours and refer the patient and family for MH testing either contracture or DNA analysis[1].

Patients who are known to be MH susceptible may be anesthetized with regional anesthesia, local anesthesia or total intravenous anesthesia. If general anesthesia or sedation is required, the inhalation agent and succinylcholine should be avoided. The machine should be prepared by flushing 10 L/min of fresh gas for up to 104 minutes for newer machines and older machines, flow 10 L/min of fresh gas for 20 minutes. Also, changing the CO2 absorbent, new breathing circuit and reservoir bag to the Y-piece of the circle system is recommended[13]. Activated charcoal filters reduce anesthetic concentrations until 5ppm for 12 hours duration in a short period of time; however, the machine should be flushed with high fresh gas flow of 10L/min for 90 seconds prior to the placement of activated charcoal filter in both inspiratory and expiratory limbs[14].

CONCLUSION

Malignant hyperthermia is an autosomal dominant disease, which is considered a life threating condition. It typically presents with a rise in the end tidal CO2, tachycardia, and hyperthermia. Every anesthesiologist must be aware of the pathophysiology of malignant hyperthermia and have the necessary knowledge and skills to prevent the occurrence of such a complication.

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