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Malignant Hyperthermia

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Introduction

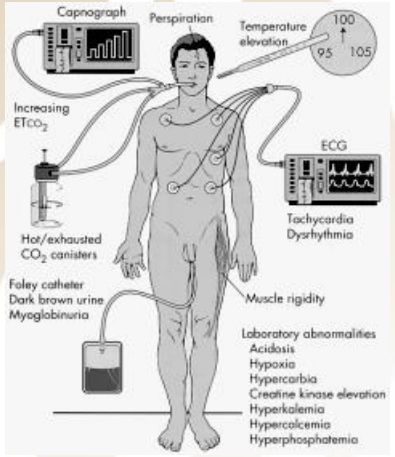
A crisis of malignant hyperthermia is a medical emergency, and must be treated immediately with a coordinated, multidisciplinary team response in order to give the patient the highest chance for a successful recovery (Dirksen, Van Wicklin, Mashman, Neiderer, & Merritt, 2013). Malignant hyperthermia is defined by Bandschapp & Girard (2012), as "a disturbance of the skeletal muscle calcium homeostasis, triggered by volatile anaesthetics and depolarizing muscle relaxants." Once a vulnerable patient is exposed to one of these triggering agents, a pathologic hypermetabolic response ensues, and the patient has a rapid increase in oxygen consumption and expired carbon dioxide, hyperthermia, acidosis, muscle rigidity, and hyperkalemia (Bandschapp & Girard, 2012).

The event of malignant hyperthermia is very rare, but can easily progress to a life-threatening situation (Cain, Riess, Gettrust, & Novalija, 2014). Many clinicians are unprepared to manage and treat the event because of its rarity and the use of low-frequency, high risk skill set (Cain, Riess, Gettrust, & Novalija, 2014). Dirksen, Van Wicklin, Mashman, Neiderer, & Merritt (2013), claim that malignant hyperthermia occurs in approximately 1:3,000-50,000 procedures in which general anesthetics are used.

Although the prevalence rate is low there is a good chance an anesthesia clinician will experience a malignant hyperthermia crisis at least once in their career and they must be aware of how to handle the situation. That is why I picked this rare topic. I am in the Nurse Anesthesia program, and providing information about this crisis can spread awareness about a situation that could directly affect my colleagues' or my own career.

The condition was termed in 1960, by Denborough and Lovell who described the disorder in a family with this autosomal dominant mode of inheritance (Bandschapp & Girard, 2012). Years later in the 1970's mortality rates for the hyperthermia crisis were still over 80%, and after years of research the pathogenesis of the complication was discovered, along with the medical treatment in dantrolene (Bandschapp & Girard, 2012).

Currently, mortality rates have decreased to less than 5% because of the symptoms being immediately recognized and treated by anesthesia clinicians (Bandschapp & Girard, 2012). Malignant hyperthermia is still a very dangerous state, yet very treatable under the proper clinician education.



(Muldoon, 2014)

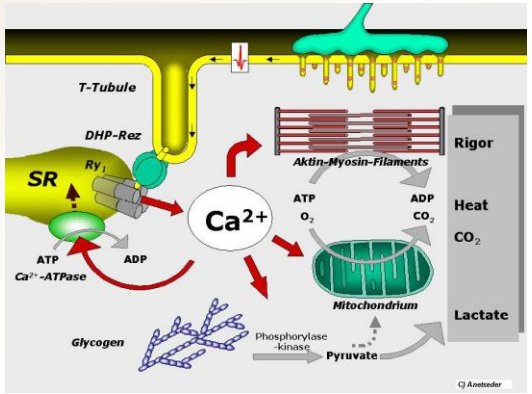
Presentation of Case

A 34 y.o. man was admitted to the hospital for a cholecystectomy. On preop assessment the CRNA found no previous surgeries and a family history of anesthetic complications, but the patient could not tell what these issues were. Surgery went well with removal of the gallbladder, successful anesthetic reversal, and no apparent complications. After surgery the patient was stable with HR, 75 bpm, BP, 127/82, RR, 16/min, O2sat, 100%, temp., 36.9 C. Upon admission to the PACU, patient's HR increases to 91 bpm, and RR, 21/min, and the nurse gives the patient 3 mg of Morphine IVP for pain and increases his oxygen delivery to 4 L NC. The nurse then continues to see increase in HR, RR, BP, and temp. After giving the patient another 3mg of Morphine IVP, and increasing his oxygen to 5L NC, the nurse calls the CRNA and surgeon to report changes in patient's condition. After this, the patient reports muscle rigidity of the trunk, displays ventricular ectopy, and vital signs are now as follows: HR: 127 bpm, BP: 167/101 mm Hg, RR: 31/min, O2sat: 89%, and body temp: 39.5 C. The CRNA, now at bedside, quickly makes the diagnosis of malignant hyperthermia and administers 2.5mg/kg of dantrolene IVP and 2 mEq/kg of bicarbonate and reintubated the patient. A cooling blanket is then applied to the patient and an ABG and labs are drawn that show: pH, 7.21; Pco2, 75 mmHg; Po2, 85 mmHg; potassium, 7.2 mEq/L. The patient is then given 10 units of regular insulin IVP, followed by 50 ml of 50% dextrose in water IV, and 10 mg/kg of calcium chloride. The patient is then transferred to the ICU unit (Anderson-Pompa, Foster, Parker, Wilks & Cheek, 2009).

This patient displays the many signs and symptoms of the post operative emergency, malignant hypothermia (MH). This is a condition that develops rapidly and must be treated immediately. This genetic skeletal muscle disorder does not always happen immediately. In some cases like this example, the signs and symptoms can occur after surgery in the recovery period (Cain, Riess, Gettrust, & Novalija, 2014). The condition results in the body developing into a hypermetabolic state with tachycardia, hyperpyrexia, muscle contractions, and changes in electrolyte and acid-base balances (Johns, Stoudt, Scholtis, & Gavel, 2012). More specific clinical signs of MH included: a rise in end-tidal CO2 and lactic acid production leading to a respiratory and metabolic acidosis, muscle spasm/rigidity, especially of the masseter muscle and truncal area, hyperthermia of above 39º C, myoglobinuria and eventually renal failure, hyperkalemia, tachycardia/tachypnea, and cardiac arrhythmias/arrests (Dirksen, Van Wicklin, Mashman, Neiderer, & Merritt, 2013). These symptoms must be recognized quickly and there must be an emergency care plan in place to treat patients displaying these symptoms.

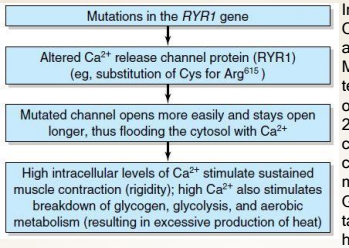
Pathophysiology and Significance

The underlying pathophysiology behind malignant hyperthermia begins with the excitation-contraction coupling mechanism where "the muscle action potential is propagated along the sarcolemmal membrane into the transverse tubule, where the dihydropyridine receptors (DHP receptor) sense the action potential voltage change and open up" (Bandschapp & Girard, 2012). The opening of the DHP receptors then activates the ryanodine recepors to open, which allows calcium to be released from the Sarcoplasmic reticulum of the muscle cells and cause muscle contraction (Bandschapp & Girard, 2012). The muscle contraction then relaxes as calcium is actively pumped back into the sarcoplasmic reticulum by the ATP-dependent calcium pump (Revello, 2012). Patients that are susceptible to MH have an autosomal dominant disorder in which they have a defect in the ryanodine receptor type 1 (RYR1) gene (Dirksen, Van Wicklin, Mashman, Neiderer, & Merritt, 2013). By pairing this abnormal ryanodine receptor gene with the presence of a triggering agent like anesthetic gasses (halothane, isoflurane, sevoflurane, desflurane, or enflurane) either alone or in combination with a depolarizing muscle relaxant (succcinylcholine), an uncontrolled calcium release from the sarcoplasmic reticulum will result as an effect of the triggering agent causing the RYR1 to remain open (Dirksen, Van Wicklin, Mashman, Neiderer, & Merritt, 2013). This calcium starts the actin-myosin troponin interaction which makes the muscle contract by shortening the muscle fibers (Dirksen, Van Wicklin, Mashman, Neiderer, & Merritt, 2013). This uncontrolled calcium release overwhelms the compensatory mechanism (calcium pump) within the cell and cause a sustained state of muscle contraction, which causes the hypermetabolic MH response (Dirksen, Van Wicklin, Mashman, Neiderer, & Merritt, 2013). Early on the muscle cells attempt to restore homeostasis through aerobic and anaerobic metabolism, however it is overpowered by the excessive amount of calcium in the myoplasm, and reaches the threshold levels for myofibrillar contraction (Revello, 2012).



(Revello, 2012)

This process is significant in that it rapidly depletes adenosine triphosphate (ATP) and increases glucose metabolism, oxygen consumption, carbon dioxide production, and heat production; as well as increases lactate production and worsens acidosis (Revello, 2012). As ATP stores become exhausted, the plasma membrane integrity lessens causing rhabdomyolysis and the leakage of myoglobin, CK, and electrolytes like potassium, phosphate, and magnesium into the circulation (Revello, 2012). This damage can cause skeletal muscle damage, renal failure, and cardiac arrhythmias or arrest (Dirksen, Van Wicklin, Mashman, Neiderer, & Merritt, 2013).



(Shrestha, 2013)

Implications

Implications must be taken especially by CRNA's to monitor and be prepared for a MH crisis. Although a classic sign of MH is pyrexia, an increase in temperature usually occurs later than other signs (Bandschapp & Girard, 2012). One of the first signs of MH is the continual occurrence of increased carbon dioxide despite increases in minute ventilation (Bandschapp & Girard, 2012). If this is noticed along with tachycardia, muscle rigidity, possible hyperthermia, diffuse perspiration, acidosis, and hyperkalemia, the CRNA or Anesthesiologist must be clued to the diagnosis of MH, and act immediately.

Once MH is suspected, all triggering agents should be discontinued including the anesthetic gas, and sedation should be changed to propofol (Bandschapp & Girard, 2012). Then help should be called, and a preplanned MH multidisciplinary team/plan should be activated and personnel should follow preset MH policies and guidelines (Dirksen, Van Wicklin, Mashman, Neiderer, & Merritt, 2013). The CRNA should then hyperventilate the patient with high fresh gas flow (>10 L/min or 1.0 FiO2), and then treat the patient with 2.5mg/kg bolus of dantrolene (Bandschapp & Girard, 2012).

(JHP Pharmaceuticals, LLC, 2014)

Dantorlene is a specific ryanodine receptor antagonist, and inhibits the increased calcium release form the sarcoplasmic reticulum, which is why it is the primary drug to treat MH (Bandschapp & Girard, 2012). The 2.5mg/kg bolus can be repeated up to 4 times until the MH signs and acidosis subside, and in some cases may require more than 10mg/kg (Bandschapp & Girard, 2012). The patient then must be packed in ice to attempt to keep the patient's temperature below 38.5 ºC. CRNAs must also regularly draw ABGs, and blood and urine labs, to check acid-base status, electrolytes, coagulation profile, creatinine, CK, and myoglobin (Bandschapp & Girard, 2012). If acidosis worsens or serum potassium climbs, an additional bolus of dantrolene should be given (Bandschapp & Girard, 2012).

CRNAs must also be attentive and monitor and treat other conditions caused by MH, like disseminated intravascular coagulation, kidney damage form the myoglobin in the blood, and rhabdomyolysis associated with electrolyte imbalances (Bandschapp & Girard, 2012). They may need to give fluids and diuretics to help clear myoglobin in the kidneys, or correct electrolyte imbalances, especially hyperkalemia. Once the condition is under control the patient needs to be transported to the intensive care unit for 36-48 hours to monitor for possible reoccurring symptoms, and 1 mg/kg of dantrolene should be continued every 4-8 hours as indicated by lab values and clinical parameters (Bandschapp & Girard, 2012).

Conclusion

Malignant Hyperthermia is a medical emergency, and although rare, every person involved in the OR team must be prepared to act quickly and accurately to give the patient the best chance for survival. The only testing for MH includes a muscle biopsy or molecular genetic testing, which are too invasive for a preoperative screen (Bandschapp & Girard, 2012). Therefore, a thorough surgical and medical history must be done on the patient to check for possible MH complications that have occurred in the family. Perioperative personnel, especially CRNAs, must be properly educated to quickly and appropriately recognize, treat, and manage a patient in a malignant hyperthermia crisis.

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