Malignant Hyperthermia (Malignant hyperpyrexia)

This is a nonexertional heat disorder occurring as an idiosyncratic reaction of skeletal muscles characterized by a hypermetabolic state that occurs in response to potent inhalation anesthetic agents and depolarizing muscle relaxants that used in anesthesia practice.

This exposure results in loss of normal calcium homeostasis within the skeletal muscles.

Inhalational agents that are associated with malignant hyperthemia include;

- Halothane,
- Sevoflurane, and
- Desflurane,

The common depolarizing muscle relaxant associated with this problem is succinylcholine (suxamethonium),

In other words, All inhalation anesthetics except nitrous oxide can trigger the development of malignant hyperthermia.

In some isolated cases, malignant hyperthemia can result due to stresses such as vigorous exercise and heat.

The genetic defect associated with malignant hyperthermia is thought to be the ryanodine receptor, coded for by a gene on Chromosome 19 and autosomal dominant in terms of inheritance.

Patients with this rare inherited defect in intracellular calcium control are asymptomatic until given succinylcholine or anesthetic vapors

Patients who have a genetic myopathy known as Central Core Disease are usually at a higher risk of developing malignant hyperthermia in case of any trigger.

Central Core Disease (CCD) is a rare non progressive myopathy with autosomal dominant inheritance, that presents in infancy and characterized by hypotonia and proximal muscle weakness.

Epidemiology of malignant hyperthermia.

Malignant hyperthemia is known to have an incidence of between 1:50,000 to 1:100,000 patients who are exposed to anesthetic agents.

This reaction develops more commonly in males than in females in the ratio of 2:1.

Succinylcholine induced masseter muscle rigidity has an incidence of 1 in 100 children to who are induced by halothane and given succinylcholine.

The incidence is probably the same following induction with sevoflurane, but much less following induction with thiopental

Signs and symptoms of malignant hyperthermia

The classic signs include

? Hyperthermia (High body temperatures)to marked degree,
? Sweating,
? Tachycardia,
? Hyperkalemia,
? Tachypnea,
? Hypercapnia (Unexplained elevation of expired CO2,)
? Increased oxygen consumption,
? Metabolic acidosis,
? Muscle rigidity especially masseter muscles noticed on intubation, and
? Rhabdomyolysis.

Malignant hyperthermia can occur at any time during or after anesthesia. These patients will develop the above features with hyperthermia being a dramatic but late manifestation.

When the condition is precipitated by suxamethonium (succynylcholine) it is more rapid and dramatic or even slower and manifesting hours after anesthesia use.

Hyperthermia is charcterized by an increase in core temperature at a rate of 1–2 degrees celcius 5 every five minutes. Severe hyperthermia of more than 44 degrees celcius may occur, and lead to a marked increase in oxygen consumption, CO2 production, vital organ dysfunction, and disseminated intravascular coagulation.

In this case of uncontrolled hypermetabolism, there is cellular hypoxia manifested by a progressive and worsening metabolic acidosis. If it remains untreated, there ensures a continuing myocyte death and rhabdomyolysis that complicates to a life-threatening hyperkalemia and myoglobinuria that may lead to acute kidney injury.

Diagnosis of malignant hyperthermia

Diagnosis of malignant hyperthermia is reached upon based on the clinical presentation of the patient and additional laboratory testing.

As mentioned prior, the main diagnostic markers of this condition are;

? Unexplained high levels of end-tidal CO2 (ETCO2) levels more than 55mmHg,
? Unexplained sinus tachycardia,
? Muscle rigidity (severe masseter muscle rigidity with difficulty opening the patient's mouth).
? Rhabdomyolysis characterized by serum CK >20,000/L, cola coloured urine, elevated urine myoglobulin.
? Hyperkalemia (plasma potassium >6mEd/L),
? Metabolic acidosis
? Myperthemia (>38.8 degrees).

? A positive family history of a consistent autosomal dominant inheritance

Differential diagnoses

The possible diagnoses include;
? Sepsis,
? Thyroid storm,
? Pheochromocytoma, and
? Iatrogenic overheating.

Particularly problematic is the unexplained hyperthermia following anesthesia. Since anesthetic gases generally inhibit the febrile response, the first sign of sepsis may be marked hyperthermia on emergence from anesthesia. Response to antipyretics as well the clinical setting is often helpful in differentiating this response from malignant hyperthermia.

The differential diagnosis of unexplained increased ETCO2 includes;

? Hyperthermia secondary to sepsis, or
? Iatrogenic warming,
? Machine valve malfunction,
? Rebreathing,
? Faulty equipment.

Malignant hyperthermia-like syndrome, may occur outside the operating room following injection of ionic contrast agents into the cerebrospinal fluid, and the neuroleptmalignant syndrome(NMS).

Management and treatment

The initial treatment of acute malignant hyperthermia crisis is the immediate discontinuation of triggering agents, hyperventilation, administration of dantrolene in doses of 2.5 mg/kg repeated as when necessary to limit it, cooling the patient by all routes available, and treating hyperkalemia.

The steps in the treatment are as follows:

1. Stop potent triggering inhalation agents and succinylcholine. You may need to maintain anaesthesia with IV agent (eg propofol); abandon surgery; muscle relaxant with non-depolarizing muscle relaxant.
2. Increase minute ventilation to lower ETCO2.
3. Call for help/stop surgery if possible
4. Prepare and administer dantrolene: at 2.5 mg/kg initial dose titrated to tachycardia and hypercarbia; with 10 mg/kg as the upper limit. Dantrolene is a skeletal muscle relaxant, which inhibits calcium release from the sarcoplasmic reticulum.
5. Begin body cooling measures: using use iced solutions such as; Ice Packs to groin, axilla, and neck, Nasogastric lavage with iced solution, tepid sponging, bladder irrigation with cold water. You should then stop cooling measures at 38.5°C. Because the temperature dysregulation is not attributable to alteration in hypothalamic set point, antipyretics such as acetaminophen, ibuprofen, and corticosteroids are ineffective at treating the condition. Haloperidol is associated with neuroleptic malignant syndrome and should not be used to treat this condition.

6. Treatment arrhythmias as needed. But do not use calcium channel blockers, since hyperkalemia may occur with such a drug combination.
7. Secure and maintain normal blood gases, electrolytes levels, creatine kinase, blood and urine for myoglobin levels;
8. Perform a coagulation profile check every 6–12 hours;
9. Treat hyperkalemia with hyperventilation with 100% oxygen, glucose and insulin as needed;
10. Continue the use of dantrolene at a dose of 1 mg/kg every 4–8 hours for 24–48 hours.
11. Insure urine output of 2 ml/kg/hour with mannitol infusion, furosemide (lasix), and fluids as needed.
12. Evaluate need for invasive monitoring and continued mechanical ventilation.
13. Observe patient in Intensive Care Unit for at least 36 hours.

Patients experiencing MH should receive dantrolene and be monitored closely for 48–72 hours, since 25% of patients will experience a recrudescence of the syndrome.

Blood coagulation profile for disseminated intravascular coagulation (DIC) should be included, as well as observation of the urine for myoglobinuric renal failure. DIC is most frequent when body temperature exceeds about 41°C.

Preventive measures

Preventive measures include a a good anesthetic history to determine the possibility of the patient or a family member having experienced an MH episode. When suspicion of MH exists, family members should not be given trigger anesthetic agents

Patients who are known to be MH susceptible may be anesthetized with regional anesthesia or local anesthesia without problems. If general anesthesia or sedation is required, the potent volatile agents and succinylcholine should be avoided.

Patients with any form of myotonia should not receive succinylcholine.

Patients with hypokalemic periodic paralysis, CCD, Duchenne or Becker muscular dystrophy, paramyotonia, or myotonia fluctuans should not receive trigger agents.

All patients receiving more than a brief general anesthetic should have their core temperature monitored.

Young patients should not receive succinylcholine for elective procedures, in order to avoid the possibility of hyperkalemic response in a patient with undiagnosed muscular dystrophy.

> The anesthesia machine should be prepared by flowing 100% oxygen through the machine at 10 L/min for at least 20 minutes