ANESTHETIC MANAGEMENT OF A PATIENT WITH HISTORY OF MALIGNANT HYPERThERMIA
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ABSTRACT: Malignant hyperthermia (MH) is a very rare life threatening condition. It has an incidence of 1:4,500 to 1:60,000 patients undergoing general anaesthesia. Disorder occurs worldwide and affects all racial groups. Clinical MH produces rapidly increasing body temperature and extreme acidosis as a result of acute loss of control of intracellular calcium levels and compensatory uncontrolled increases in skeletal muscle metabolism that may proceed to severe rhabdomyolysis. MH has a mortality rate of about 10%. We report a rare case of 59 year old male patient with history of malignant hyperthermia posted for laproscopic cholecystectomy and its perioperative management.

KEYWORDS: Malignant hyperthermia, Dantrolene, Laparoscopic Cholecystectomy, Difficult Airway, Thoracic Epidural.

INTRODUCTION: Malignant hyperthermia (MH) is an example of a pharmacogenetic clinical syndrome. It is an inherited dangerous illness characterized by a hyper metabolic state which is triggered when the person is exposed to certain anaesthetic drugs.1 Susceptible patients have a genetic predisposition for the development of this disorder, which does not manifest until they are exposed to triggering agents or stressful environmental factors. All volatile inhalational anaesthetic agents are the most commonly implicated pharmacologic triggers of MH. The overall incidence of MH during general anaesthesia has been reported as 1 in 3,000 to 15,000 children and 1 in 50,000 to 100,000 adults. MH usually occurs in children and young adults (the incidence of acute MH is highest in the first three decades of life) but has been reported at the extremes of age, ranging from infants in the delivery room to 70 years.2

The clinical manifestations of MH after exposure to anaesthetic agents are nonspecific and include tachycardia, hypercarbia, acidosis, glycolysis, hypoxemia, and heat production. This indicates a hypermetabolic condition due to sustained muscle contraction which is believed to be due to a reduction in the reuptake of calcium by the sarcoplasmic reticulum necessary for termination of muscle contraction.1

CASE REPORT: A 59 year old male patient, weighing 90 kilograms, came with chief complaints of pain in right hypochondriac region since 3 days, with nausea and vomiting since 2 days. After investigations he was diagnosed with acute symptomatic cholelithiasis due to gall bladder stones. Laproscopic cholecystectomy was advised. His medical history revealed seasonal bronchial asthma requiring salbutamol inhaler during winter and hypertension with good control on Amlodipine 5mg.
His past surgical history called our attention to a note from his previous anaesthesiologist mentioning that at the age of 14 when the patient was undergoing surgery for chronic tonsillitis he developed an abnormal reaction to succinylcholine given to intubate his trachea which was suggestive of MH. Further surgical history revealed septoplasty for deviated nasal septum in 1998 under local anaesthesia and hemorrhoidectomy for piles under subarachnoid block in 2006. There was no family history of anaesthetic related morbidity or mortality.

Preoperative examination revealed an obese patient with BMI of 31.4 with short neck and double chin, Tempromandibular (TM) distance <6.5 and Mallampatti score of 2. We anticipated difficult intubation, but Succinylcholine had to be avoided and this was a challenge faced by us.

All blood investigations were within normal limits. Pulmonary function tests were suggestive of early small airway disease with FEV₁ of 75%. Echocardiography suggested mild concentric left ventricular hypertrophy with ejection fraction of 60%. Thyroid function tests and urinary vallinyl mandelic acid levels were done to rule out thyrotoxicosis and pheochromocytoma respectively. They were found to be within normal limits.

**Anaesthetic Management:** In view of the patient’s childhood anesthetic history with general anesthesia, we considered him as a possible case for developing MH intra operatively.

As a precautionary measure we made Inj. Dantrolene available (dose- 2- 2.5mg/kg.) along with other standard resuscitation equipment. Cold intravenous solutions and cooling blankets were also made available. We planned for balance Anaesthesia: Thoracic Epidural for Analgesia and General Anaesthesia with controlled ventilation.

Patient received tablet alprazolam 0.5 mg on the night prior to surgery followed by morning dose of anti hypertensives and nebulization with Asthalin. He was wheeled into the operation theatre- Continuous EKG, non-invasive blood pressure, pulse oxymetry, end tidal carbondioxide (EtCO₂) and temperature monitors were attached to the patient. Baseline readings were normal. Lactated ringers solution (500ml) was started through a 18 gauge (G) Intravenous (IV) access.

Right sided Internal jugular vein cannulation was done with double lumen catheter for central venous pressure (CVP) monitoring. Baseline CVP was 8 centimetres of water (cm H₂O).
CASE REPORT

Nasogastric tube and Foley’s self-retaining catheter inserted. Thoracic Epidural along with General Anaesthesia was planned. In sitting position under all aseptic precautions, 18 G Epidural catheter was inserted with 18 G Epidural needle at T10-11 space after confirming loss of resistance, the catheter was fixed at 12cm from skin. Test dose with Inj. Ropivacaine 0.2% 3ml given after negative aspiration for blood and cerebrospinal fluid (CSF). Twenty ml of Ropivacaine was administered into the Epidural space with the patient in supine position. Top ups were given hourly.

General Anaesthesia: With difficult Airway Cart in place, patient was pre oxygenated with 100% oxygen for 3 minutes.

Premedication: IV Injection (Inj.) Glycopyrrlate 0.2 mg, Inj. Fentanyl 150 microgram (µg) and Inj. Midazolam 2.0mg.

Induction: Inj. Propofol 160 mg IV and muscle relaxant Inj. Rocuronium bromide 60mg IV.

Intermittent positive Pressure Ventilation (IPPV) was done for 90 sec, after jaw relaxation, laryngoscopy was done. Intubation was difficult as the laryngeal opening was quite anterior and the laryngoscopic view could be best labeled as Cormach Lehane grade-2. With the help of Talwalkar’s bougie, 8.5 cuffed endotracheal tubes was passed through. Bilaterally equal air entry was checked, cuff inflated and fixed. Depth of anaesthesia was maintained with O₂(40%), N₂O (60%) and Propofol infusion at 40ml per hour using closed circuit ventilatory machine with pressure control mode and ventilatory setting as Tidal Volume-550, respiratory rate-14, Inspiration: Expiration ratio 1:2. Relaxant used was Inj. Rocuronium 60mg (induction dose) +40mg (10mg top ups were given every 30 minutes, a total of 100mg). Inj.Pantoprazole 40mg IV, Inj. Ondansetron 8 mg IV, Inj. Hydrocortisone 100mg IV and Inj. Dexamethasone 8mg IV were also given prophylactically in view of bronchial asthma. Surgery lasted for 150 minutes. Continuous monitoring of vitals showed no alarming change and patient was extubated after regaining his spontaneous respiration and protective reflexes with reversal inj.Neostigmine 3.0mg IV +Glycopyrrolate 0.5mg IV. Patient was shifted to the recovery for 24 hours of monitoring. He received postoperative analgesia with epidural infusion of 50ml Ropivacaine 0.2% 40 ml+Fentanyl 100µg+6ml normal saline at the rate of 6 ml per hour over the period of 24 hours along with Paracetamol 1gm IV in 100ml infusion, 8 hourly. Patient was discharged from the hospital on the 5th postoperative day.

DISCUSSION: Malignant hyperthermia is a disorder that manifests as a life-threatening hypermetabolic crisis in susceptible individuals after exposure to inhalational anaesthetics. Anyone who is involved with anesthesia must have an up to date knowledge on its pathophysiology, prevention, diagnosis and treatment of this potentially dangerous condition. Here we discuss the clinical features, differential diagnosis, and management guidelines for a patient susceptible to MH, undergoing surgery.
A Manif | B Manifestation
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Respiratory acidosis | End-tidal CO₂ >55 mmHg, PaCO₂ >60 mmHg
Cardiac involvement | Unexplained sinus tachycardia, ventricular tachycardia, or ventricular fibrillation
Metabolic acidosis | Base deficit >8 mEq/L, pH <7.25
Muscle rigidity | Generalized rigidity, severe masseter muscle rigidity
Muscle breakdown | Serum creatinine kinase concentration >20,000/L units, cola-colored urine, excess myoglobin in urine or serum, plasma [K+] >6 mEq/L
Temperature increase | Rapidly increasing temperature, T >38.8° C
Other | Rapid reversal of MH signs with dantrolene, elevated resting serum creatinine kinase concentration
Family history | Consistent with autosomal dominant inheritance

Table 1: Clinical findings in malignant hyperthermia and its manifestation

From Larach et al [1994], Rosenberg et al [2002]

A. Clinical findings (except family history) are in order of relative importance.
B. Signs occurring during or shortly after general anesthesia in the untreated individual.

The diagnosis of malignant hyperthermia is based on:
1) Clinical presentation
2) Contracture test
3) Genetic studies

Clinical presentation as per documentation with the patient was suggestive of MH. Since the contracture studies are not being done in India it was not possible to do a standardized caffeine-halothane contracture test in this patient. Genetic testing for malignant hyperthermia is not available in India presently and could not be done in this patient. This was a limiting factor in our study. The combination of hypercarbia, muscle rigidity, tachycardia, hyperthermia, metabolic acidosis, and rhabdomyolysis during or shortly after anesthesia is distinctive for MH. Some syndromes share some elements of MH: Sepsis, Overheating from aggressive heating measures utilized during anesthesia, Pheochromocytoma crisis, Ischemic encephalopathy, Ascending tonic-clonic syndrome, Thyrotoxicosis, Neuroleptic malignant syndrome (NMS), Dystrophinopathy, Myotonic syndromes.

Anesthesia for patients with known MH susceptibility must be done only with non-triggering anesthetics. Evading all triggering agents is mandatory. (see table 2)
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- Unsafe drugs
  - Depolarizing muscle relaxants (succinylcholine)
  - Inhalational agents (cyclopropane, methoxifluorane, halothane, enflurane, isoflurane, sevoflurane, desflurane)
- Insufficient data / controversial
  - d-Tubocurarine
  - Phenothiazines
- Safe drugs
  - Antibiotics
  - Antihistamines
  - Antipyretics
  - Barbiturates (thiopental, methoexital)
  - Benzodiazepines (midazolan, diazepam, lorazepan)
  - Droperidol
  - Ketamine (inherent circulatory effects may mimic MH)
  - Local anesthetics (lidocaine, bupivacaine, ropivacaine)*
  - Nitrous oxide
  - Nondepolarizing muscle relaxants (pancuronian, rocuronium, vecuronium)
  - Opioids (morphine, meperidine, fentanyl, sufentanyl)
  - Propofol
  - Propranolol
  - Vasoactive drugs

Table 2: Unsafe and safe drugs in MH patients

From Whizar-Lugo Victor et al [2004]

Management of MH susceptible patients is based of prophylactic measures as mentioned in Table 2. If general anaesthesia needs to be used, follow the steps listed in table 3.

- Extensive preoperative anesthesia evaluation
- Prepare anesthesia machine; remove all vaporizes, replace CO2 canisters, bellows, and gas hose.
- Flush anesthesia machine for 30 minutes with oxygen 10 L/min.
- Bring the MH cart inside the OR (this cart contains all supplies to resuscitate patients with MH, including dantrolene)
- Always scheduled your patient as the very first case of the day, and notify the post anesthesia care unit and the intensive care unit to be prepare to make available the necessary manpower
- Check CPK and ABG preoperatively, intra operatively and immediately in postoperative period.
Always consider several anesthetic possibilities; regional anesthesia, local anesthesia, plexus anesthesia, monitored anesthesia care, sedative techniques.

- If general anesthesia is used avoid known triggering drugs and consider total intravenous anesthesia.
- An early sign of malignant hyperthermia is a rapidly rising end tidal carbon dioxide, especially if it is unresponsive to hyperventilation. ETCO$_2$ monitoring is mandatory.
- After surgery, continue to monitor laboratory values. Keep your patient properly monitored in a safe environment.
- Advice the OR, recovery room an intensive care personal of your MHS patient.

Table 3: Management of MH susceptible patients

From Whizar-Lugo Victor et al [2004]

As soon as a MH crisis is suspected, all trigger agents should be stopped. Besides symptomatic treatment, high-flow O$_2$, termination/postponement of surgery, dantrolene sodium should be given at 2 mg/kg i.v. and repeated until the cardiac and respiratory systems stabilize.$^6$ Early dantrolene administration may decrease the 35% MH morbidity rate.$^7$

Our patient presented with a history of malignant hyperthermia, during a previous surgery. Keeping in mind his genetic predisposition and we took all necessary precautions by avoiding the triggering factors and keeping dantrolene readily available.

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