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RESEARCH ARTICLE

ANESTHETIC MANAGEMENT OF MALIGNANT HYPERTHERMIA

***Dr. Uzmagulzar and Dr. Rames. I. Talele**

Department of Anesthesiology, A.C.P.M. Medical College, India

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ABSTRACT

Malignant hyperthermia is rare inherited disorder in our part of the world; there are only few cases reported in literature in India who were suspected of having this condition. The overall incidence of malignant hyperthermia during general anesthesia is estimated to range from 1: 5000 to 1: 50,000–100,000 and mortality rate is estimated to be <5% in the presence of standard care. In India, there is no center where in vitro halothane caffeine contraction test is performed to confirm diagnosis in suspected cases. Second, dantrolene drug of choice for this condition is not freely available in market in India and is stored only in some hospitals in few major cities. Among the cases reported of suspected of malignant hyperthermia in India almost 50% have survived the condition despite nonavailability of dantrolene emphasizing role of early detection and aggressive management in these cases.

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INTRODUCTION

Malignant hyperthermia is a relatively rare disease in India with very few case reports present in the literature in this regard. Malignant hyperthermia was brought into attention for anesthetic world by deaths attributable to general anesthetics in a family living in Melbourne, Australia (Denborough and Lovell, 1960). Incidence of malignant hyperthermia during general anesthesia is estimated to range from 1: 5000 to 1: 50,000–100,000 (Rosenberg *et al*., 2007; Rosero *et al*., 2009). The mortality rate is estimated to be <5%, with early detection of malignant hyperthermia episode, using capnography, prompt use of the drug dantrolene, and the introduction of diagnostic testing (Rosenberg *et al*., 2007).

Case report

45 year female operated for cholelithiasis. On preanesthetic evaluation, patient had no comorbid condition. On the day of surgery, venous access was established minimum basic monitoring was attached to the patient. Her blood pressure was 130/80 mmHg, heart rate 78 beats/min and oxygen saturation were 98% on the operation table on room air.Induction done on propofol and scholine and was maintained 50% oxygen + air and isoflurane with atracurium. Ten minutes into surgery rise in endtidal CO_2 was noticed, adjustment in minute ventilation, circuit check, but endtidal CO_2 continued to rise up to 95 mmHg. Rise in temp (104 F), HR (190), BP(188 mmHg), respectively. Suspecting malignant hyperthermia isoflurane was stopped propofol infusion was started, and patient was ventilated with 100% oxygen through a fresh circuit. Surgeon was informed and asked to expedite surgery. Active cooling was started with ice cold saline intravenously and irrigation through Ryles tube and bladder catheter. Ice packs and cold towels were used for surface cooling.. Blood gas sample at this time : pH-7.12, pCO_2-96 mmHg, pO_2-224 mmHg, base excess-6, HCO_3-20 mEq/L, Na-142 mEq/L, and K 4.5 mEq/L suggestive mixed respiratory and metabolic acidosis. Dantrolenecould not be used due tonon availability in our hospital. With active cooling patients temperature stabilized and then started to drop toward normal. With high minute ventilation and higher flows end tidal and $PaCO_2$ were also controlled and then started to drop. Sodium bicarbonate was given to correct acidosis .Surgery was completed within 2 h and patient was shifted to Intensive Care Unit for postoperatively management. Blood samples including thyroid function test and urine for myoglobin sent from Intensive Care Unit were within normal limits. The patient was extubated after 2 h of ventilation once endtidal CO_2 temperature and acid-base status returned to normal and patient achieved criteria for extubation. Patient and her attendants were made aware of suspected diagnosis of malignant hyperthermia in her and risks of recurrence in the patient and other family members on future exposure to anesthesia. The episode was also mentioned in anesthesia record of the patient for future reference.

Corresponding author:* **Dr. Uzmagulzar,
Department of Anesthesiology, A.C.P.M. Medical College, India

Table 1. Malignant hyperthermia clinical grading scale

Clinical indicators	Points
Muscle rigidity	
Generalized rigidity	15
Masseter rigidity	15
Process II:Myonecrosis	
Elevated CK>20,000(after succinylcholine administration)	15
Elevated CK>10,000(without exposure to succinylcholine)	15
Cola colored urine	10
Myoglobin in urine>60mg/l	5
Blood/plasma/serum K>6mEq/l	3
Process III: Respiratory acidosis	
PETCO2>55 with controlled ventilation	15
PAC02>60 with controlled ventilation	15
PETCO2>60with spontaneous ventilation	15
Inappropriate hypercarbia	15
Inappropriate tachypnea	10
Process IV: Temperature increase	
Rapid increase in temperature	15
Inappropriate temperature>38.8^{0}C in perioperative period	10
Process v: Cardiac involvement	
Inappropriate tachycardia	3
Ventricular tachycardia or fibrillation	3
Others	
Arterial base excess more negative than -8mEq/L	10
Arterial Ph<7.25	10
Rapid reversal of malignant hyperthermia signs of metabolic and/or respiratory acidosis with iv dantrolene	5

Table 2. Clinical significance of malignant hyperthermia raw score and its rank (Larach *et al*., 1994)

Raw Score Rank	Malignant hyperthermia	Description of likelihood
0	1	Almost never
3-9	2	Unlikely
10-19	3	Somewhat less than likely
20-34	4	Somewhat greater than likely
35-49	5	Very likely
50+	6	Almost certain

Table 3. Malignant hyperthermia score in patient

Clinical indicators	Points
Arterial paco2> 60mmHg with appropriately controlled ventilation	15
$PETCO_2$ > with controlled ventilation	15
Rise in temperature >39.9^{o}C (104^{o}F) in perioperative period	10
Arterial blood pH>7.25	10
Inappropriate tachycardia	3
Masseter spasm shortly after succinylcholine administration	15
Total score	68

DISCUSSION

Malignant hyperthermia is a myopathy associated with abnormal skeletal muscle calcium homeostasis in response to triggering agents such as succinylcholine andisoflurane. Sustained high levels of calcium insarcoplasmic reticulum lead to increased aerobic and glycolytic metabolism leading to acidosis, rigidity, altered permeability, and hyperkalemia (Saxena and Dua, 2007). Diagnosis of malignant hyperthermia is based on clinical parameters at the time of crisis which is later confirmed by muscle biopsy test. Larach *et al*. (1994) described a scoring system tolabel a patient of hypermetabolic crisis as malignant hyperthermia using different patient parameters during this crisis (Tables 1 and 2). According to this grading, a patient with a score >50 points is definitely a case of malignant hyperthermia. Our patient had a score of 68 points (Table 3) which was highly suggestive of malignant hyperthermia in this patient. Furthermore, other causes of hypermetabolic crisis such as thyroid storm, neuroleptic malignant syndrome, and pheochromocytoma were ruled out by normal thyroid function test, patient not being on any antipsychotic drugs and having no history suggestive of pheochromocytoma.

For definitive diagnosis of malignant hyperthermia in vitro halothane caffeine contraction test is used (Gupta and Hopkins, 2010). This test has to be done after 3 months of hypermetabolic crisis (A protocol for the investigation of malignant hyperpyrexia (MH) susceptibility, 1984) genetic research into the condition implicate the ryanodine receptor gene (RYR1) located on chromosome 19 (McCarthy *et al*., 1990; MacLennan *et al*., 1990) as cause of malignant hyperthermia. DNA testing is now used routinely for diagnosis before muscle biopsy when a familial RYR1 mutation is known (Urwyler *et al*., 2001). First case of malignant hyperthermia in India was reported in 2001 by Punj *et al*. (2001) patient developed a gradual increase in heart rate, PaCO2, temperature 44°C, pH 7.17, bicarbonate concentration 19.7 mmol/L, potassium concentration 6 mmol/L, and creatine kinase concentration 29,900 IU/L. Followed by disseminated intravascular coagulation with hematuria and patient died 12 h after the initial episode. Similar cases were reported by Gupta *et al*. (2012) and Pillai *et al*. (2015) who succumbed in spite of aggressive supportive measures. Saxena and Dua (2007) and Gopalakrishnan *et al*. (2010) also reported cases who survived the episode of malignant hyperthermia without use dantrolene as was the case in our patient. Currently, there is no center in India which performs IVHCT, so we were not able to offer it to the patient in order to confirm the diagnosis of malignant hyperthermia. Dantrolene, the drug of choice for this disease, is not freely available in market is stocked in only few hospitals in our country. Hence, could not be used in this patient as it was not available in our hospital. Although license for import of dantrolene can be obtained within few days dantrolene is not available in market due to its limited use, its cost, and storage facility needed for the drug. Since more cases of malignant hyperthermia have been recorded in people of Indian subcontinent descent in the United Kingdom than in India, this discrepancy may suggest lack of essential monitoring, as may be the case in some peripheral centers and nonavailability of accredited diagnostic center for diagnosis (Larach *et al*., 1994).

Conclusion

Early awareness and proper management even in the absence of dantrolene can improve survival. Furthermore diagnostic center and dantrolene should be made available in order to have best chance of survival.

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