Case Report

Successful management of malignant hyperpyrexia syndrome in a pediatric patient: What to do when dantrolene is not available?

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ABSTRACT

Malignant hyperpyrexia syndrome (MHS) is a rare entity and may not be encountered by the anaesthesiologists throughout their professional career. Whenever it manifests can be a challenging task to manage and prove to be fatal when a timely diagnosis and required therapeutic measures are not taken. Althoughthe dantrolene should be available wherever anaesthesia is practiced, considering the rarity of the syndrome this may not be the scenario always. We are reporting a case of MHS in a pediatric patient to highlight the facts that prompt clinical diagnosis, ongoing supportive treatment, discontinuation of all the anaesthetic agents and and stringent perioperative monitoring along with postoperative oral dantrolene may provide an answer to the MHS crisis in the face of an unavailability of the IV dantrolene; as may be the case in many rural and developing set-ups.

Key words: Dantrolene, malignant hyperthermia, oral dantrolene, ryanodine receptor, supportive management

INTRODUCTION

Malignant hyperpyrexia syndrome (MHS) is a rare life-threatening entity characterized by rapid rise in body temperature, heart rate and muscle rigidity triggered by an exposure to certain anesthetic agents like succinylcholine and volatile anaesthetics. We present a case of MHS in a 10-year-old girl emphasizing that a prompt identification, rational symptomatic and supportive therapy until the availability ofthe dantrolene sodium can be lifesaving.

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CASE REPORT

A 10-year-old girl (18 kg) was scheduled for an open reduction internal fixation of the fracture shaft of right humerus. A detailed preanaesthetic checkup revealed no significant past or family history. After obtaining written informed consent from the parents, the patient was wheeled into the operation theatre followed by an application of a pulse oximeter (SpO_2). The inhalational induction was conducted with 100% Oxygen (O_2) and 8% sevoflurane using Jackson Rees Ayre T–Piece (JRM-ATP) circuit. The sevoflurane was reduced to 4% after initial 4-5 breaths and then to 2%. After the loss of consciousness, a 22-gauge intravenous

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line was secured and a non-invasive blood pressure and electrocardiography (ECG) leads were applied. Injections fentanyl 40 µg, propofol 40 mg and vecuronium bromide 2 mg were administered intravenously (IV) followed by an intubation with a 5.5 cuffed endotracheal tube. A circle system with volume control mode of ventilation was used with a tidal volume, respiratory rate and inspiration: Expiration of 150 milliliters, 18/min and 1:2, respectively. After induction, the end tidal CO_2 ($ETCO_2$) and nasopharyngeal temperature were also monitored. The sevoflurane was replaced with halothane after 20 min of anaesthesia and intraoperative vitals were maintained within normal limits throughout the surgical time of 45 minutes. At the end of surgery, the patient bit the tube while the peak airway pressures and $ETCO_2$ increased suddenly. Considering the possibility of a light plane of anesthesia, propofol 20 mg and succinylcholine 5 mg IV were administered. This was however followed by an increased jaw tone: Rise in the $ETCO_2$ to a maximum of 190 mmHg over 10 min and core temperature to 107°F (41.67°C). These with hypertonicity of the limbs and an unexplained tachycardia of 200-210 beats per minute (bpm) suggested a diagnosis of MHS. The IV dantrolene sodium was neither available in the hospital nor in any nearby pharmacy. The supportive management was started and IV lidocaine 1.5 mg/kg bolus was administered which decreased the heart rate (HR) to 170-180 bpm. IV amiodarone was given in a loading dose of 3 mg/kg followed by an infusion @ 1 mg/kg/hour. The whole body cold sponging was done and the operation theatre (OT) temperature was decreased to 20°C. The circuit was replaced with a new JRM-ATP circuit; the vaporizer and sodalime were bypassed and 100% O_2 was used. The ECG started showing tall T waves and an arterial blood gas (ABG) revealed a combined respiratory and metabolic acidosis [pH-6.8, PCO2-169 mmHg, PO2-200 mmHg, potassium-7 milliequivalents/liter (meq/l) and sodium- 135 meq/l]. A glucose insulin drip was started with 10% dextrose plus 10 unit insulin @ 50 ml/h and sodium bicarbonate was administered in a dose of 2 meq/kg. IV furosemide 1 mg/kg was given to maintain the urine output.

The supportive management was continued for 3hours. The patient's HR settled down to 100-110 beats per minute while the temperature, $ETCO_2$ and ECG returned to normal. As the patient started having respiratory effort the neuromuscular blockade was reversed with neostigmine and glycopyrrolate. The trachea was extubated and the patient was shifted to the pediatric intensive care unit (PICU) for further observation and management. Meanwhile, serum creatine phosphokinase (CPK) was checked which was found to be markedly elevated (25000 U). The thyroid function tests and a repeat ABG and serum electrolyte were in the normal range. The IV dantrolene sodium could not be arranged but oral dantrolene sodium capsules were made available after 6 h of long search at various pharmacists. The oral dantrolene was administered in a dose of 25 mg three times a day orally for 3 days.

The patient was shifted to the ward after 3 days and finally discharged home with a note indicating that she suffered from an episode of MHS during general anaesthesia and her parents were sensitized to inform the concerned anesthesiologist about this event, next time whenever she is posted for a surgery.

DISCUSSION

MHSis an autosomal dominant disorder triggered by an exposure to certain anaesthetics agents in susceptible individuals with a mutation at the ryanodine receptor gene RYR1.[1,2] This leads to a greatly increased intracellular calcium release due to a lowered activation and heightened deactivation threshold.[3,4] The increased intracellular calcium activates the myosin ATPase resulting in an increased ATP consumption, O_2 consumption, CO_2 production, hyperthermia and rigidity.[5,6]There are no simple signs, symptoms or tests demonstrating a susceptibility to the MHS, which can occur even hours following an exposure to a triggering agent.[7] Dantrolene sodium, a hydantoin derivative and muscle relaxant act directly on the RYR1 to prevent calcium release from the sarcoplasmic reticulum and is the drug of choice for the treatment of MHS. It is used in doses of 2 mg/kg every 5 min to a maximum of 10 mg/kg.

Our patient was a 10-year-old girl from a rural background with no personal or family history suggestive of a susceptibility to the MHS. All the classical signs such as masseter spasm (biting of the tube), increased rigidity of the limbs, a rapid and sudden rise in the body temperature (107°F, 41.67°C), tachycardia (200-210 bpm), hypercapnia (190 mmHg), respiratory acidosis (PH 6.8) and hyperkalemia (7 meq/l) were in accordance with the established diagnostic criteria for the MHS.[7] Later, ECG changes suggestive of hyperkalemia appeared followed by the ventricular tachycardia (VT) for which IV lignocaine was given and an amiodarone infusion was started in view of persistent VT. The temperature was brought down by surface cooling and decreasing the OT temperature to 20°C. An early control of temperature and hyperkalemia is of vital importance but prolonged cooling after achieving normal body temperature must be avoided, otherwise dangerous hypothermia with loss of central temperature control can occur. The $ETCO_2$ returned to normal after some time. To compensate for an increased O_2 consumption and CO_2 production hyperventilation with 100% O_2 was done. As malignant hyperthermia can reoccur postoperatively, the patient was observed in the PICU for 3 days.

The muscle cell damage due to ATP depletion and increased temperature can lead to hyperkalemia, myoglobinemia, increased creatine phosphate and creatine kinase. IV furosemide was given to provoke the renal excretion of potassium and myoglobin. Calcium must not be used in this condition as RYR1 are calcium sensitive. The patient was investigated for the CPK, ABG, serum electrolytes and thyroid function tests. Markedly elevated levels of the CPK confirmed our diagnosis of the MHS. The caffeine halothane contracture test could not be conducted due to its unavailability in our hospital and poor economic condition of the patient. This case report highlights that the clinical judgment, an ongoing supportive treatment, discontinuation of all the anesthetic agents and stringent perioperative monitoring along with oral dantrolene may provide an answer to the MHS crisis in the face of an unavailability of diagnostic tests and timely availability of the IV dantrolene; as may be the case in many rural and developing set-ups. However, this is not to undermine that the dantrolene should be available as a standard of care wherever anesthesia is practiced. A markedly high level of CPK indicated that this child has a high tendency for developing MHS next time whenever she is exposed to the triggering agent. Therefore, the plan for removal of K-wire would be preoperative dantrolene prophylaxis, total intravenous anesthesia (TIVA), use of a new anesthetic circuit along with the bypass of the vaporizer and sodalime.

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Conflicts of interest

There are no conflicts of interest.

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