Case Report

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Malignant Hyperthermia in Pediatric Patients: A Case Report of Successful Management

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ABSTRACT

Malignant hyperthermia (MH) is a rare and life-threatening inherited skeletal muscle disorder, often triggered by mutations in the ryanodine receptor gene (RYR1). These mutations can cause muscles to become excessively sensitive to certain anesthetics (such as halothane, sevoflurane, isoflurane) and muscle relaxants like succinylcholine, resulting in elevated body temperature, muscle rigidity, metabolic disturbances, and other severe physiological responses. Early identification and prompt, aggressive intervention are essential for effectively managing malignant hyperthermia. In this case, we illustrate a successful outcome involving a 3-year-old child who developed malignant hyperthermia during a tonsillectomy procedure after exposure to sevoflurane. Postoperative genetic testing confirmed the presence of the RYR1 gene mutation.

Keywords: Malignant Hyperthermia; RYR1 Mutation; Sevoflurane; Case Report

Abbreviations: ICU: Intensive Care Unit; CK: Creatine Kinase; MH: Malignant Hyperthermia; RYR: Ryanodine Receptor 1; CRRT: Continuous Renal Replacement Therapy

Introduction

Malignant Hyperthermia (MH) is a rare genetic muscle disorder that can be triggered by routine inhalational anesthetics or muscle relaxants like succinylcholine. This leads to muscle rigidity, high body temperature, and a hypermetabolic state. MH is the only known inherited disorder linked to perioperative mortality from anesthetic drugs. The estimated incidence of MH is 1:10000 to 1:25000 [1], and without timely diagnosis and treatment, it can have a high mortality rate [2]. In China, reported mortality rates for MH can reach 45.7% [3], with children being more vulnerable than adults [4]. Clinical manifestations of MH vary, and failure to promptly recognize it can contribute to the high mortality rate [5]. In a comprehensive survey conducted in China, it was found that only 23.5% of anesthesiologists were able to correctly identify an increase in end-tidal carbon dioxide as the initial symptom of Malignant Hyperthermia (MH). The majority (69.1%) mistakenly believed that a rapid elevation of body temperature was the primary indication [5]. This lack of prompt recognition by most anesthesiologists can result in delayed treatment, putting patients' lives at risk. In March 2024, our hospital effectively managed a case of malignant hyperthermia in a pediatric patient. Despite the lack of dantrolene sodium, the child responded well to a combination of physical cooling, sedation, and hyperventilation. This report outlines the onset and treatment of the patient's condition.

Case Data

The patient, a 3-year and 7-month-old male weighing 16kg and measuring 98cm, presents with a chief complaint of 'snoring during sleep with mouth breathing for the past six months' and a preoperative diagnosis of obstructive sleep apnea. The planned procedure is elective tonsillectomy and adenoidectomy. Preoperatively, the patient has a temperature of 36.3°C, heart rate of 121 beats per minute, and is classified as ASA grade I. All preoperative laboratory test results are within normal limits. On February 28, 2024, following appropriate preoperative preparations, the patient was escorted to the operating room. Upon arrival, vital signs were documented as non- invasive blood pressure of 102/60mmHg, heart rate of 116 beats per

minute, and pulse oxygen saturation of 99%. At 08:45, intravenous anesthesia was initiated with 30ug fentanyl, 60mg propofol, 20mg rocuronium bromide, 2mg atropine, and 2mg dexamethasone sodium. Endotracheal intubation was successfully performed post- induction of intravenous anesthesia, with symmetrical bilateral breath sounds identified.

Mechanical ventilation commenced in pressure-control mode at 12 cmH2O, utilizing a tidal volume of 160ml, respiratory rate of 22 breaths per minute, and an end-tidal carbon dioxide partial pressure (PetCO2) of 40mmHg. Anesthesia maintenance throughout the surgery included inhalation of sevoflurane (1.5%), continuous intravenous infusion of propofol at 0.12 mg·kg-1·min-1, and remifentanil at 0.01 ug·kg-1·min-1. At 10:45, the patient experienced a sudden and significant rise in PetCO2, reaching 99mmHg in just five minutes. This was accompanied by a rapid increase in heart rate, peaking at 150 beats per minute. Initial assessment revealed symptoms such as facial flushing, sweating, skeletal muscle rigidity, and elevated skin temperature upon palpation, prompting concerns of malignant hyperthermia. Inhalational anesthesia was promptly halted, and the breathing circuit along with the soda lime canister were replaced. High-flow oxygen was administered to address hyperventilation, while rectal temperature monitoring showed a reading of 40.3°C.

Prompt initiation of symptomatic treatment was carried out. The treatment protocol includes rapid cooling through intravenous infusion of cold saline, application of ice packs to specific areas such as the neck, axillae, groin, and popliteal fossa, and alcohol wiping of the patient's entire body. Acidosis is corrected through hyperventilation, internal environment stability is maintained, and circulatory function is closely monitored. The PetCO2 started to decrease at 11:05, reaching 40mmHg by 11:20, while the temperature dropped to 38.5°C around 11:50 and heart rate decreased to 121bpm. Blood gas analysis at 11:25 revealed mild metabolic acidosis with a pH of 7.31, arterial PaCO2 of 42.8mmHg, and a base excess (BE) of -4.2mmol/L. By 12:00, the patient regained consciousness, and the endotracheal tube was removed. Continuous monitoring took place until 12:30, when the patient was transferred to the Intensive Care Unit (ICU) for further care. Throughout the ICU stay, the patient's body temperature remained elevated, fluctuating between 39.2°C and a maximum of 40.2°C. Additionally, there were signs of rhabdomyolysis, as indicated by increased creatine kinase (CK) levels and myoglobinuria (urine analysis on the first postoperative day showed ketones 3+, CK- MB 28.9IU/L, and elevated infection markers such as white blood cells). With appropriate treatment, liver function tests, complete blood counts, and cardiac troponin levels gradually returned to normal. Whole-exome sequencing was conducted on the patient and his mother with the family's approval. The results identified a point mutation (amino acid alteration) on the RYR1 gene: c.1021G>A (p. Gly341Arg), linked to susceptibility to Malignant Hyperthermia type (MIM:145600) (Figure 1).

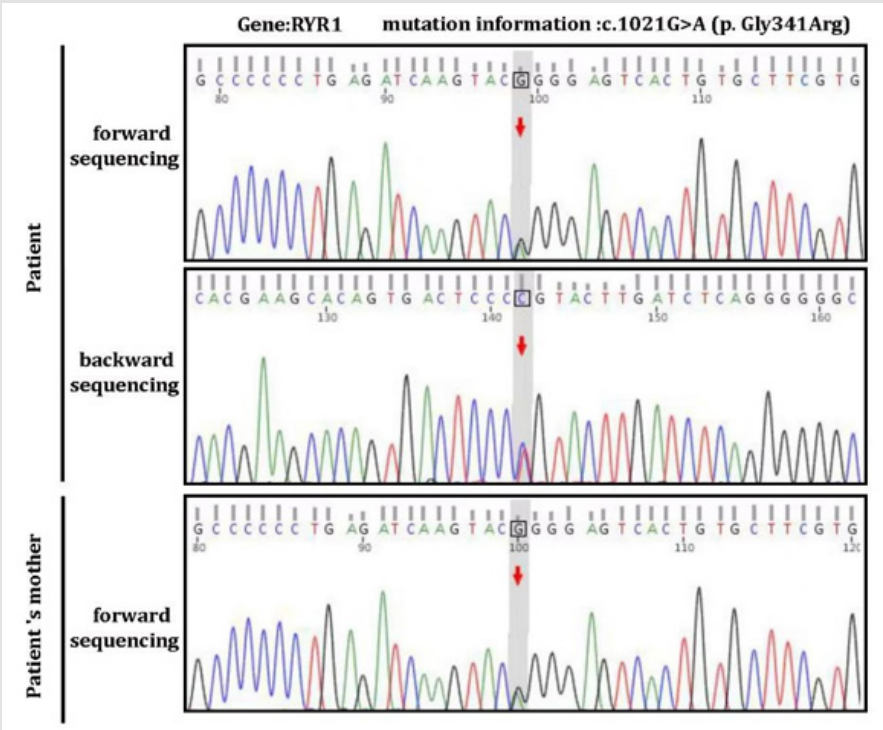

Figure 1: Exons group sequencing display appear RYR1 gene point mutation (amino acid): c.1021G > A (p. Gly341Arg).

Discussion

Malignant Hyperthermia (MH) is a condition characterized by abnormal metabolic hyperactivity and skeletal muscle spasms triggered by exposure to inhalational anesthetics and depolarizing muscle relaxants. It typically manifests suddenly and can occur in the operating room or during anesthesia recovery, presenting as a rapidly progressing and potentially fatal condition. Common clinical signs include sudden onset hypercapnia, significant elevation of body temperature (up to 45°C–46°C), skeletal muscle rigidity, hyperkalemia, tachycardia, abnormal blood pressure, rapid breathing, altered consciousness, sweating, peripheral leukocytosis, and elevated enzyme levels such as creatine kinase, lactate dehydrogenase, and aspartate transaminase. The patient experienced a sudden increase in PetCO2 and elevated heart rate as initial intraoperative symptoms. Other potential causes of hypermetabolic states, such as hyperthyroidism, pheochromocytoma, infection, transfusion reactions, and certain nonspecific drug reactions like neuroleptic malignant syndrome, were ruled out. Suspecting malignant hyperthermia, immediate symptomatic treatment was initiated, including cooling, sedation, and hyperventilation, leading to rapid temperature reduction. Effective cooling measures likely played a crucial role, with a prompt response and timely interventions resulting in normal electrolyte and coagulation parameters without serious complications.

Furthermore, replacing the breathing circuit and soda lime canister helped prevent residual absorption of anesthetic drugs. It is essential to highlight the importance of temperature monitoring when suspecting malignant hyperthermia, even though it may partially delay the timely detection of changes in the patient's condition. Following stabilization of the patient, whole-exome sequencing was conducted on both the patient and his family members to detect mutations in the RYR1 gene [6,7]. Studies have validated that mutations in the ryanodine receptor 1 (RYR1) gene are responsible for the majority of cases of Malignant Hyperthermia (MH). These mutations cause abnormalities in the skeletal muscle sarcoplasmic reticulum, leading to elevated calcium levels when patients are exposed to triggering factors like inhalational anesthetics, resulting in prolonged skeletal muscle contraction. MH is an autosomal dominant disorder, with offspring of MH patients having a 50% risk of inheriting the condition. Hence, it is essential to educate individuals on how the test results could impact their health insurance, job prospects, and even relationships. Dantrolene, a specific treatment for Malignant Hyperthermia (MH), effectively inhibits the release of calcium ions from the sarcoplasmic reticulum, inducing muscle relaxation [8].

Early administration of dantrolene can reduce perioperative mortality in MH. Challenges such as the low incidence of MH, difficulties in storage leading to potential drug ineffectiveness and wastage, and the lack of cost-benefit analysis regarding the reserve of dantrolene have resulted in over half of anesthesiologists lacking understanding of the optimal timing and preparation methods for dantrolene [5]. This highlights the importance of continuous temperature monitoring for patients receiving inhalational anesthesia or depolarizing muscle relaxants, prompt diagnosis, and early treatment. Hospitals should ensure they have such special treatment drugs in stock to be prepared for emergencies. If immediate availability of dantrolene is not possible, there are several key issues to consider in managing MH. Early detection and diagnosis of MH are critical, as timely identification and treatment are essential for a successful outcome. Rapid mobilization of multidisciplinary teams throughout the hospital is a vital component of MH management.

Various cooling methods should be employed, including extracorporeal circulation cooling if needed, to quickly lower body temperature below the danger threshold. CRRT plays a significant role in maintaining internal balance, correcting electrolyte imbalances and acidosis, stabilizing hemodynamics, and effectively removing myoglobin and inflammatory agents. Adjusting the temperature of replacement fluids can aid in cooling patients during hypermetabolic states and preventing/treating renal failure. Initiation of heparin therapy early can decrease consumption of clotting factors and platelets in DIC, while guaranteeing hemodynamic stability and administering corticosteroids and diuretics as required. As a final option for patients experiencing ongoing cardiac arrest, ECMO may be utilized. Due to the rarity of MH and limited experience in many healthcare facilities, rescue operations can be incredibly challenging. Establishing timely and effective communication with anesthesia specialists from other institutions for expert guidance is imperative for successful rescue missions.

Conclusion

Although rare in China, Malignant Hyperthermia (MH) has been successfully treated despite some shortcomings in rescue and monitoring methods. MH is known for its rapid onset, high mortality rates, and various complications. The use of dantrolene has shown to significantly improve patient outcomes. In cases where dantrolene is not readily available, it is crucial to implement appropriate symptomatic treatments such as continuous renal replacement therapy (CRRT), physical cooling, brain protection, and ECMO support therapy as needed. It may be advisable for hospitals or regions to consider stocking dantrolene as a routine practice.

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