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Case Report / Olgu Sunumu

Post-Operative Malignant Hyperthermia in a Child after Colon Interposition

Çocukta Kolon İnterpozisyonu Sonrası Postoperatif Malign Hipertermi

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Abstract / Öz

Malignant hyperthermia (MH) is a rare and potentially life threatening fatal complication of anaesthesia. We present a 2-year-old boy with late onset MH after colon interposition to replace the oesophagus under sevoflurane anaesthesia. The patient was treated with intravenous dantrolene sodium as well as cooling and controlled ventilation. Despite treatment, the patient developed cardiopulmonary arrest at 21 hours after the operation and died. It should be kept in mind that post-operative MH may develop during these types of operations with ischaemia-reperfusion injuries.

Keywords: Malignant hyperthermia, general anaesthesia, post-operative hyperthermia, colon interposition

Malign hipertermi (MH) nadir, hayatı tehdit eden ve ölümcül olabilecek bir anestezi komplikasyonudur. Biz iki yaşında erkek çocukta sevofluran anestezisi altında özafagus yerine kolon interpozisyonu sonrası geç başlangıçlı MH sunduk. Hasta intravenöz dantrolen sodyum, soğutma ve kontrollü solunumla tedavi edildi. Tedaviye rağmen girişimden 21 saat sonra hastada kardiyopulmoner arrest gelişti ve hasta exitus kabul edildi. İskemi reperfüzyon hasarıyla ilgili bu tür operasyonlarda postoperatif MH nin gelişebileceği akılda tutulmalıdır.

Anahtar kelimeler: Malign hipertermi, genel anestezi, postoperatif hipertermi, kolon interpozisyonu

Introduction

Malignant hyperthermia (MH) is a hyper metabolic response of skeletal muscles triggered by potent inhalation agents, the depolarizing muscle relaxant succinylcholine and stresses such as anaesthesia duration, pain, physical stimulation, fear and heat. Although, it generally occurs after the induction of general anaesthesia, it may also appear after any operation. MH is a well-known clinical entity but post-operative event is not clearly understood. In this case, report, we describe the clinical characteristics of a patient in whom the signs and symptoms of acute MH began in the post-operative period. We also discuss the possible etiological factors.

Case Presentation

A 2-year-old boy weighing 10 kg was scheduled for colon interposition. He had congenital oesophageal atresia. The family history was non-conclusive for anaesthetic problems or neuromuscular disorders. He had undergone general anaesthesia four times previously for oesophagostomy and gastrostomy procedures with sevoflurane, vecuronium and fentanyl, without experiencing any adverse events. Written informed consent was obtained from the patients' parents before surgery. On the day of operation, physical and laboratory examinations were within normal limits. Anaesthesia was induced by intravenous 1-μg kg^{-1} fentanyl, 2-mg kg^{-1} propofol and 0.1-mg kg^{-1} vecuronium. Anaesthesia was maintained with sevoflurane, fentanyl and vecuronium to obtain stable haemodynamic parameters. The duration of the surgery was approximately 7 hours. No respiratory or haemodynamic problems occurred during anaesthesia. The blood loss was minimal. Standard fluid therapy was administered. His urine output was 3.1 mL kg^{-1} h^{-1}. After extubation, the patient was admitted to the intermediate care unit with stable vital signs. Initially, laboratory examinations were normal in the post-operative period. The axillary temperature changed irregularly between 37°C and 38.5°C and blood cultures were taken. Anti-pyretic agents and symptomatic treatment was administered. Five hours after the operation, mechanical ventilation was initiated with a pressure-controlled mode because of respiratory and circulatory deterioration. Dopamine and dobutamine of 5 μg kg^{-1} min^{-1} infusions were

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immediately started. While the patient was being monitored, generalised tonic–clonic seizures were observed. To treat this, we used rectal diazepam (0.5 mg kg^{-1}), phenobarbital (20 mg kg^{-1}), phenytoin (10 mg kg^{-1}), midozolame infusion and valproic acid (20 mg kg^{-1}). As there was no response, a sodium thiopental infusion (0.3 mg kg^{-1} h^{-1}) was started and seizures were controlled after 3 hours. Simultaneously, supraventricular tachycardia was seen on the electrocardiogram; therefore, adenosine (0.3 mg kg^{-1}) was given 3 times with gradually increasing doses; metoprolol (0.1 mg kg^{-1}) was applied because of the persistent supraventricular tachycardia. In addition, there was no change in rhythm. Despite 10-J and 20-J direct current cardioversion, p waves were not seen. Sinus rhythm returned after a second metoprolol dose. The body temperature (BT) was 39.50°C. Sepsis criteria were not observed and the initial surgical antibiotic prophylaxis was continued. Eight hours after the operation, the BT increased from 39.50 to 41°C in 60 min. The BT changes are shown in Figure 1. The analysis of blood gases showed that $PaCO_2$ reached 36.7 mmHg despite a 75% increase in minute ventilation (8 L/min) and demonstrated the following results: pH: 7.25, PO_2: 201 mmHg, SpO_2: 100%, BE: –11.2 mmol L^{-1}, HCO_3^-: 15.2 mmol L^{-1}, K^+ (3.50–4.50): 3.8 mmol L^{-1} and ionic Ca^{2+} (4.49–5.29): 3.8 mg dL^{-1}. Arterial blood gas analysis indicated metabolic acidosis. Cola colour was detected in the urine. Urine output gradually decreased and finally stopped. At this point, the patient was evaluated as having MH. According to a clinical grading scale for MH introduced by Larach et al. (1), the total score was 55 and the patient was ranked as D6 (almost certain).

Until his symptoms were controlled, a total of 40-mg dantrolene sodium (1 mg kg^{-1}) was administered at 4 hours by multiple boluses. Surface cooling continued. Bladder and gastric irrigation with ice cold water was conducted. After 4 hours, the patient's BT was returned to normal and urine output started. The following results were obtained from the blood tests: blood urea nitrogen: 79 mg dL^{-1}, creatinine: 1.78 mg dL^{-1} and creatinine kinase: 1750 U L^{-1}. Urine examination revealed that blood reaction (+3) and myoglobulinuria were present. The patient continued to deteriorate as BT increased even with continued intensive therapy for MH. Twenty-one hours after the operation, the patient developed cardiopulmonary arrest and died. Blood cultures were later found to be negative.

Discussion

Malignant hyperthermia may begin in the post-operative period (2, 3). Some disorders mimic MH. However, when considering the clinical features of our patient, some clinical entities including neuroleptic malignant syndrome, hyperthyroidism and pheochromocytoma have to be ruled out. There were no fluid and electrolyte imbalances, sepsis or other metabolic and neurological problems in our patient. At this point, we thought that the most rational method was to tend to the Larach scale. On the other hand, when the literature is carefully examined, it can be seen that MH could develop without any increase in the end-tidal carbon dioxide

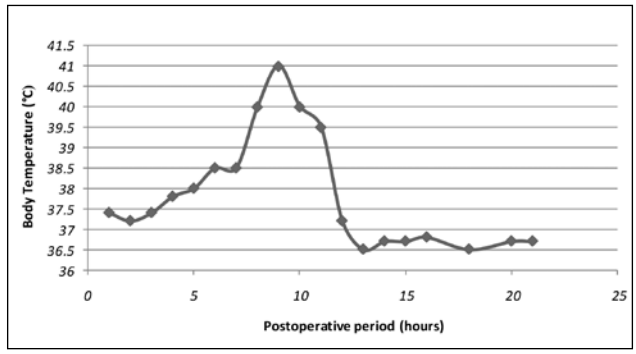

Figure 1. Changes in the body temperature following the operation

(CO_2) concentration even though the CO_2 retention takes place commonly in MH (4).

We think that there are three possible explanations for the late-onset post-operative symptoms. Firstly, volatile anaesthetic agents, such as sevoflurane and desflurane, may have a tendency to increase the risk of MH. Recent studies suggest that the volatile anaesthetic sevoflurane increases myoplasmic calcium release via the ryanodine receptor (RYR1) as well as by inositol 1,4,5-triphosphate stimulation (5). We used sevoflurane anaesthesia, and it should be considered as a risk factor for MH in this case.

Secondly, genetic factors are undoubtedly important in the pathophysiology of MH. Family history is not essential to the development of MH (5). In our case, we already had no positive family history. Linkage studies have implicated the RYR1 locus on the chromosome 19q12–13.2 (1).

The gold standard in the diagnosis for MH susceptibility (MHS) is the *in vitro* contracture test with halothane and caffeine (IVCT) (1). Unfortunately, the caffeine-halothane contracture test is not standardised in our hospital and there was no family history. Therefore, we did not require any tests for MH pre-operatively.

Thirdly, environmental stresses have been reported to trigger MH in patients with MHS. Grinberg et al. (3) presented post-operative MH episodes in three patients who had received 'safe' anaesthetics. While the pathogenesis of stress-induced MH is not clear, it may be related to the stress and pain induced by light anaesthesia.

Malignant hyperthermia is related to the uncontrolled release of intracellular calcium from the sarcoplasmic reticulum of skeletal muscles (1). Ischaemia-reperfusion injury can trigger accelerated calcium release from the skeletal muscle. Although it has not been stated in the literature, reperfusion injury is a risk factor of MH. However, we speculate that a reperfusion injury could have been the triggering factor for MH in our case.

Conclusion

Malignant hyperthermia may more likely develop, particularly during operations for ischaemia-reperfusion injury.

Triggering agents for MH in anaesthesia induction should be more carefully chosen in these patients. Pain control protocols should be organised post-operatively.

Informed Consent: Written informed consent was obtained from patients' parents who participated in this case.

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