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Case Report Open Access

Postoperative Malignant Hyperthermia Following Appendectomy

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Introduction

Malignant Hyperthermia (MH) is a rare perioperative complication triggered by volatile anesthetic gases such as halothane, sevo flurane and the depolarizing muscle relaxant succinylcholine [1-3]. The pathophysiologic changes of MH are due to uncontrolled rise of myoplasmic calcium, which activates biochemical processes related to muscle activation [4,5]. The estimated incidence of MH is between 1:50000 and 1:150000 anesthesias [1]. Most of MH cases exhibits clinical symptoms during operations, and postoperative MH is uncommon [6,7]. The latency period between the anesthesia finish time and the onset of a sign indicative of MH is estimated in the range from 0 to 40 min [7]. The present report describes a case of MH which presented clinical symptoms around 4 hours after an emergent appendectomy, and was diagnosed as "almost certain" by The Clinical Grading Scale [8].

Case Report

A 40-year-old male was referred to Omori Red Cross hospital because of abdominal pain for several hours. His Body Mass Index (BMI) was 27.5 kg/m^2 (165 cm, 75 kg). The pain localized in the right lower quadrant and there was diaphoresis and mandible thrill on arrival. Physical examination revealed tenderness on pressure in the right lower quadrant, but there was no muscular rigidity. He had a low grade fever of 37.3°C,100 beats/min, and 168/123 blood pressure. He had suffered from hypertension and gastroesophageal reflux disease, but he had no history of neuromuscular disease and surgical operations. Also, he had no significant family history. He had been a heavy drinker and a smoker. Hematological examination revealed white blood cells 13500/mm^3, Glutamate Oxaloacetate Transaminase (GOT) 55 IU/L, Glutamate Pyruvate Transaminase (GPT) 69 IU/L, and γ-glutamyl transpeptidase (γ-GTP) 449 IU/L. Other laboratory results were in normal range. A Computed Tomography (CT) scan demonstrated a swelling of the appendix with an elevated concentration of surrounding fat, making a diagnosis of acute appendicitis (Figure 1). Then, an emergent appendectomy was performed via pararectal incision. Anesthesia was induced with 200mg of propofol and sevoflurane, followed by 70 mg of rocuronium bromide for endotracheal intubation. No abnormal muscular sign was observed during induction of anesthesia. Furthermore, during the operation, vital signs didn't change significantly, as shown in Figure 2. Body Temperature (BT) was stable around 39°C. During the operation, droperidol, sugammadex sodium, lidocaine, flurbiprofen axetil were dosed. The anesthesia and operation times were 2 hours and 32 minutes, and 2 hours and 6 minutes, respectively. The blood loss was 38 g, and the total infusion volume of Ringer's solution was 1700 ml. Urine output was 600 ml, and urine was clear with no abnormal findings. On arrival in the postoperative ward, the patient's blood pressure was 136/89 mmHg with a pulse of 98 beats/min, and his BT was 36.5°C. No abnormal neuromuscular sign was seen. However, 4 hours after the operation, hyperthermia (BT 41.5°C), tachycardia (maximum HR was 190 beats/min), diaphoresis, muscular rigidity throughout the body, and disturbance of consciousness were suddenly emerged. Those symptoms faded out gradually. A brain CT scan showed normal image, and an abdominal CT scan showed abdominal incisional hernia probably due to extraordinary muscular rigidity. On the next day, hematological examination revealed that creatinine kinase (CK) (25764 IU/L, CK-MB was in normal range (8.0IU/L)), GOT (20817 IU/L), GPT (5054 IU/L), Lactate Dehydrogenase (LDH) (13110 IU/L), fibrin degradation products (FDP) (101.9 mg/dl), and CRP (10.91 mg/dl) were remarkably elevated, and that, on the contrary, platelet (29000/μl) and prothrombin percentage activity (31%) were remarkably decreased. There was no abnormal blood gas analysis (pH 7.430, PaO_2 96.6 mmHg, $PaCO_2$ 37.7 mmHg, Base excess 1.5 mmol/L). The MH score defined by Larach was 53 and MH rank was 6, which means the qualitative likelihood was "almost certain". Furthermore, almost all symptoms and laboratory analysis of MH occurred. Hence, MH and Disseminated Intravascular Coagulation (DIC) were clinically diagnosed. We immediately started administration of dantrolene sodium and thrombo modulin. BT dropped gradually and hematological data got better day by day (Figure 3). Between 1 and 4 postoperative day, visual and auditory hallucination and monology revealed, and disappeared on the 5 postoperative day. There was no muscular symptom could be found during hospitalization after the appearance of muscular rigidity. Finally the patient was discharged on the 22 postoperative days. After 5 months from the initial operation,

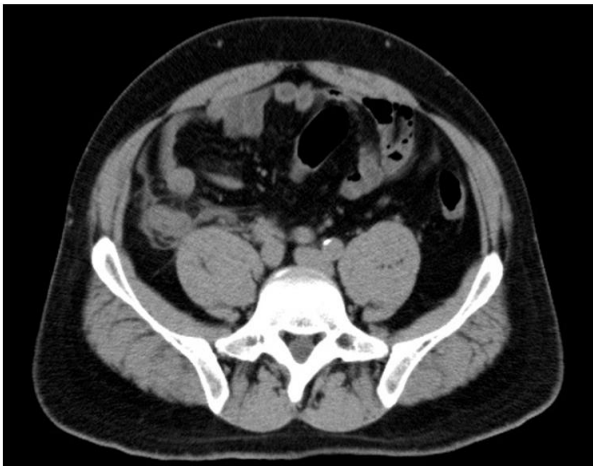

Figure 1: A Computed Tomography (CT) scan demonstrated a swelling of the appendix with elevated concentration of surrounding fat.

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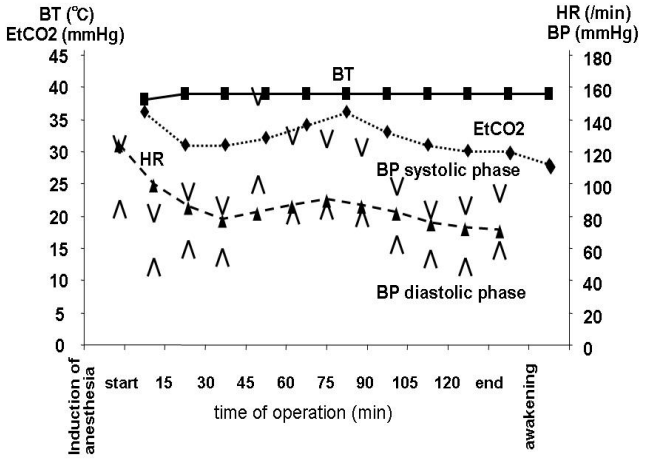

Figure 2: Vital signs during the operation. Body Temperature (BT), end-tidal carbon dioxide (ETCO2), Heart Rate (HR), and systolic and diastolic Body Pressure (BP) are shown.

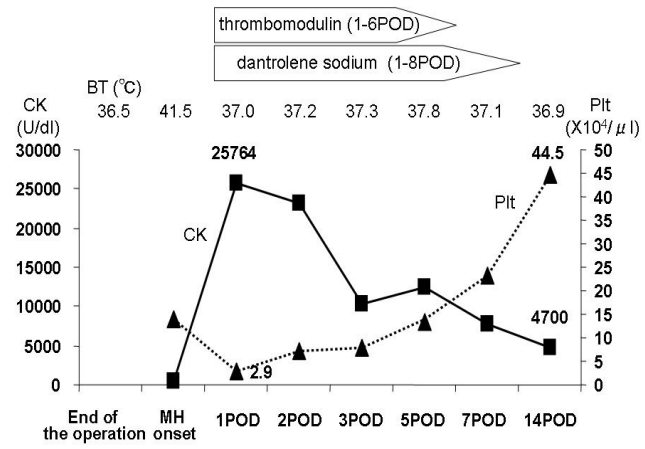

Figure 3: Postoperative change in body temperature (BT), creatinine kinase (CK), and platelet (Plt) are shown. Figures of their parameters got gradually better by the administration of thrombomodulin and dantrolene sodium.

abdominal incisional hernia repair was performed. At the same time, some portion of the rectus abdominis muscle was resected and applied for Calcium Induced Calcium Rate (CICR) test at the Saitama medical university. CICR test exhibited normal range.

Discussion

The incidence of MH is estimated between 1:50000 and 1:150000 anesthesia's [1]. Most of MH cases exhibits clinical symptoms during operations, and only few cases of postoperative MH have so far been reported [6,7], and their incidence was estimated about 1.9% among suspected MH cases. Although the diagnosis of MH is based on clinical presentation or laboratory analysis, the predisposition to MH has not been clear and we cannot preoperatively predict which patients are at risk of MH. Inoperative management with prudent caution for MH is needed for early diagnosis of MH [9]. The Clinical Grading Scale was developed by Larach et al. in order to assist in clinical diagnosis [8]. This patient's MH score was 53 and MH rank was 6, which means the qualitative likelihood was "almost certain". Almost all symptoms and laboratory analysis of MH occurred in this case. In Japan, clinical diagnostic criterion drawn up by Morio et al. has been used to diagnose MH [10]. This criterion stresses to high grade fever during anesthesia or rapid elevation of body temperature, and our case was categorized into "postoperative abortive MH" In our case, the first clinical sign was tachycardia, and secondly hyperthermia, tachypnea, and rigidity. Whether an elevation of end-tidal carbon dioxide (ETCO2) concentration that is one of the principal diagnostic features of MH appeared or not was unclear. The variability in the order and time of onset of signs and no specific clinical sign of MH make the clinical diagnosis rather difficult, especially when the events are postoperatively occurred. The difficulties of diagnosis could make starting of appropriate treatment delayed, while the most important point of treatment is to start at early phase of MH. Hence, we should not hesitate to start the treatment as soon as MH is suspected. Specific therapeutic drug for MH is dantrolene sodium which inhibits Sarcoplasmic Reticulum (SR) Ca^{2+} release [11].

MH is a hyper metabolic response to potent inhalation agents, the depolarizing muscle relaxant succinylcholine, and rarely, in humans, stresses such as vigorous exercise and heat. These triggers accelerate CICR system, and lead to uncontrolled release of intracellular calcium from skeletal muscle SR. The enhanced intracellular calcium results in activation of muscle contraction, oxygen consumption, carbon dioxide production, ATP breakdown and heat. In almost all cases, the MH susceptible patients have a defective calcium channel located in the SR membrane, termed the ryanodine receptor (RYR) [12]. The channel is closely associated with other proteins and structures, such as the di hydropyridine calcium channel that mediates transfer of voltage change to the RYR-1 receptor. Although mutations associated with MH susceptibility are found mainly in the gene for the RYR-1 [13,14], several mutations in other genes have so far reported. However, in most cases of MH, responsible mutations have not been identified [12]. In this case, CICR test exhibited normal range, suggesting that mechanism of skeletal muscle calcium release might not be associated with RYR because this test reflects the function of Ca^{2+} homeostasis including RYR of SR in skeletal muscle. Other genes' mutations or polymorphisms could be associated with the onset of disease. Yuge and Mukaida performed CICR test for 43 patients with an episode of postoperative MH, and CICR rate of 42 patients was in normal range [15]. This result supports our hypothesis, and suggests that the pathogenesis of postoperative MH might be different from that of classical MH.

We used dantrolene sodium to treat the patient of postoperative MH. The most important thing when we suspect that MH is occurred is to administer dantrolene sodium to the patient as soon as we can. Dantrolene sodium reduces fever production in skeletal muscle by directly interfering with muscle contraction through the inhibition of calcium-ion release from the SR [11]. In addition, dantrolene sodium has no life-limiting side effect that inhibits administrating.

Postoperative MH is a very rare complication, and its diagnosis from clinical presentation is very difficult. Actually, the mechanisms or clinical manifestations of MH have not been cleared, but MH could be one of life-threatening complications. We must keep in mind the possibility of MH onset even after any operation, and make immediately an appropriate treatment even for suspicious cases. And further accumulation of MH cases and more detailed molecular biological analysis are needed.

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