International Clinical and Medical Case Reports Journal
Research Article (ISSN: 2832-5788)

Malignant Hyperthermia Developed During Cardiac Pacemaker Operation

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Citation: *Sinem Bahar Celebi, Specialist of Anaesthesiology and Reanimation, Istanbul, Turkey. Int Clinc Med Case Rep Jour. 2024; 3 (6):1-7.*

Received Date: 24 June, 2024**; Accepted Date:** 06 July, 2024**; Published Date:** 08 July, 2024

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BACKGROUND

Malignant hyperthermia (MH) is a rare but a terminal autosomal dominant myopathy that generally develops through inhalation anesthetics and/or depolarizing neuromuscular blocking agents. It has been associated with 70% ryanodine receptor gene mutation. MH crisis is as a result of malfunction in intracellular calcium mechanism, which is due to muscle rigidity and increasing in body temperature (1^{o}C / 5 min.) that may advances to dissemine intravascular coagulation disorder (DIC), and its incidence is 1:14000-200000. MH is seen more common in men than women, and half of the reported cases consist of pediatric patients[1] . In this phenomenon 17-year-old female patient with congenital heart disease is presented, and while anesthesia was maintaining with sevoflurane during her permanent cardiac pacemaker installation operation, MH crisis was suspected. Since lack of dantrolene in our center, we could not give dantrolene to the patient, however thanks to the early and sufficient supportive care, she was discharged without remaining of any sequel. Although the patient was operated under general anesthesia before, it is noteworthy that the MH crisis has not been mentioned at patient's anamnesis.

PRESENTATION OF PHENOMENON

The 17-year-old, 60-kg patient with congenital heart disease had four trouble-free operations under general anesthesia which inhalation anesthetic were used: At the age of 5, the patient got operation for Atrioventricular Canal Defect (AVCD); at the age of 6, the patient got operation for tonsillectomy; at the age of 14, the patient got emergency intraabdominal bleeding operation as a result of car accident; at the age of 16, as a result of developing cardiac block after the AVCD operation, installation of permanent cardiac pacemaker. Fifteen days before the MH crisis, subcutaneous area that the cardiac pacemaker was placed got infected, so the pacemaker was removed under anesthesia. During this stage, end-tidal value increased to 60 mmHg, and redness and sweating occurred in head and neck area. This situation continued about 45 minutes and interpreted as Red Neck Syndrome that is a side effect of vancomycin. The surgically installation of permanent cardiac pacemaker was planned for the patient and she was taken to the operating room, EKG and saturation monitorization was done, and two peripheral venous ways

were opened with 18 G cannula and 20 G cannula urinary catheter. With 20G cannula, arterial blood pressure was followed continuously. In the beginning, the heart rate of the patient was 80/min., and arterial blood pressure was 110/72 mmHg. After the intravenous induction with sodium thiopental, midazolam and rocuronium bromide, the patient was intubated with 7.0 mm cuffed endotracheal tube (ET) without encountering any problem. The received blood gas values were within normal limits, so surgical operation was started and anesthesia continued with inhalation anesthetic (sevoflurane). After about 30 minutes, progressive increase in end-tidal carbon dioxide (CO_2) values observed which cannot stopped by hyperventilation. Surgical operation was stopped stating that there was a problem with patient's hemodynamic, inhalation agent was stopped and the patient was given 100% oxygen via external oxygen tube. When the patient's ET area wanted to be controlled, it was seen that masseter muscle spasm was developed and ET was compressed. Rocuronium bromide, fentanyl and midazolam were added in order to relax the patient. The airway of the patient was released with the installation of airway, but upon recognizing the redness and sweating on patient's face, her body temperature was measured from her forehead and the result was 38°C. Suspected with malignant hyperthermia (MH), support personnel were called. By placing the oral heater probe, core heater was followed. Central catheter was placed and liquid infusion was started at +4°C. Cold plates were put on the major arteries track ways of the patient and on the head. Her surgery covers were wetted and the surgery room was cooled. Nasogastric was installed and cold lavage was done. After all this efforts to cool the patient, her esophagus temperature was still 40°C and it was increasing. Thereupon, to cooling the patient's blood temperature with extracorporeal membrane oxygenation (ECMO) was planned. Blood gas was received at intervals and pH values at 7.2 were intervened with sodium bicarbonate and calcium. Furosemide was performed in order to avoid the fluid overload and possible myoglobinuria damage. Even though the patient's maximum heart rate was 100/min. because of complete cardiac block as a result of previous operation, various arrhythmias were still observed. Initially the blood pressure was 180/110 mmHg; however after it's gradually decreased to 55/35 mmHg, then 10mcg/kg/min dose dopamine infusion was initiated. There is no dantrolene in our hospital. Our patient was 60 kilogram. Ten vials of 2.5 mg/ kg iv dose of dantrolene were needed, however only one vial was found from another center which was five-minutes away from our hospital. The patient's temperature started to decrease after reaching 40.9°C and her blood gas values and hemodynamic was stabilized; therewith ECMO was not initiated. The patient was followed in surgery room until normothermia was reached, and then she was transferred to pediatric cardiovascular surgery intensive care unit. In order to diagnose a possible MH crisis earlier, the patient was followed 24 hours under intubated and sedated with sodium thiopental infusion. The next day, the patient's hemodynamic was stabile, so she was extubated. After the extubation, the patient was, cooperative and orientated, and she had extensive asthenia and muscle pains. At the second hour of

extubation, increasing body temperature was taken under control by cold application and paracetamol, and then body temperature remained at 38.5°C, so dantrolene brought form another hospital was not applied. The creatine kinase (CK) values of the patient's blood samples are presented in the Table 1 below. While checking the patient's previous values, it was seen that CK value was 11572 U/L approximately 15 days ago, after the general anesthesia applied for cardiac pacemaker removal operation. So, it was concluded that the previously experienced end-tidal CO_2 increase and flushing type redness on the face shall be interpreted as MH crisis. After the 3rd day in intensive care unit, the patient's hemodynamic was stable and she did not experience any temperature increase, so the patient was transferred to the service. The patient was discharged from hospital at the 10th day of hospitalization, but post-hospital controls revealed that the patient was experiencing extensive myogenic pain and muscle weakness, especially in lower extremities.

DISCUSSION

We did not consider the possibility of developing MH since the patient had had five operations before under general anesthesia and the patient's anamnesis did not contain any specific allergies except her allergy to vancomycin. For this reason, the end tidal CO_2 increase occurred at the beginning of the operation made us think about the ventilation problem at first place. However, symptoms like increasing body temperature, sweating and masseter muscle rigidity directed us to the malignant hyperthermia diagnosis. Red Man syndrome (Red Neck syndrome) is an allergic reaction that is characterized by erythematous rashes around face, neck and upper part of the body related with histamine increase upon applying intravenous vancomycin. The previously given vancomycin caused rashes on face and upper part of the body of the patient. For this reason, the patient may really developed Red Man syndrome against vancomycin. However, the symptoms come to existence during the operation did not show similarities with Red Man syndrome. The presentation of phenomenon published by Mathur et. al. revealed that 6-month-old female patient was applied a general anesthesia for the first time when she was hospitalized urgently for intussusception, and MH occurrence ratio in pediatric patients is 15000-200000/1[2]. Since our patient had been applied general anesthesia before, we did not consider the risk of developing MH. The study of MacKay et. al. based on 17-year-old male patient which was operated for traumatic C5 break. The patient was applied total intravenous anesthesia (TIVA), and after neuromonitorization was achieved, operation was continued under inhalation anesthesia. 45 minutes later, ETCO2 increase started[3]. In our case, however, we performed induction with intravenous anesthetic pharmaceuticals, and later we continued with inhalation anesthetic. 30 minutes later, $ETCO_2$ increase started. Under same situation, MacKay et. al. diagnosed their patient with MH and gave the patient dantrolene. Although the required dose for our patient was 10 vials of dantrolene, since we did not have any dantrolene in our center, we could only give 1 vial of dantrolene to the patient. Right now, we do not have enough information regarding the effectiveness of 1 dose of dantrolene. The Caffeine Halothane Contracture test (CHCT) is accepted as the gold standard test for establishing the diagnosis of malignant hyperthermia (MH)[3]. Skeleton-muscle biopsy for required for this test and its specificity is changing according to the center it is performed. However, this test cannot be done

in our country. For this reason, we established the diagnosis of malignant hyperthermia with the help of Larach clinical grading scale[4]. Rigidity, muscle spasm, respiratory acidosis, increase in body temperature and cardiac rhythm disorder is evaluated with this grading scale and scores higher than 50 is seen as "In all likelihood MH"; and our patient's score was 128.

RESULT

MH is observed during anesthesia applications and in case of lack of early diagnosis and supportive care, it may be terminal. If the muscle spasm cannot be stopped, this situation induces the increase in the body temperature and causes and irreversible damage in the body. For this reason, it is of vital importance to apply dantrolene during the crisis which is a pathophysiological antagonist of MH. Even though we could not supply the dose that is determined in the literature, we believe that 1 vial of dantrolene was effective on release of muscle spasm. We are also aware of the importance of early diagnosis of MH, removing the anesthetic agent and thoroughly applying the supportive care. For this reason, in terms of the survival of the patient, we would like to emphasis the importance of anesthesia and reanimation experts suspecting from non- inspiratory $ETCO_2$ and increasing body temperature, additionally immediately calling for assistance and starting supportive care. In addition, we experienced with this patient that although the previous exposure to triggering agents was known, we still cannot eliminate the risk of MH. For this reason, we are of opinion that dantrolene should be stocked for the centers that use the known triggering agents and the necessary supportive care should be kept ready before the application of general anesthesia.

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