Case Report

Prompt Treatment of Malignant Hyperthermia during Induction of Anesthesia: Case Report

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Malignant hyperthermia [MH] with high mortality is common despite the widespread use of dantrolene. The authors reported a case of a 16-year-old female with congenital lordoscoliosis, scheduled for posterior approach scoliosis surgery, developing MH during induction of anesthesia using fentanyl, propofol, cisatracurium, nitrous oxide, and desflurane. The prompt diagnosis with the aid of capnography was based on clinical symptoms of abrupt tachycardia and hypercapnia. Dantrolene was administered within 15 minutes and continued for 48 hours. Symptoms gradually subsided over the next 15 minutes and the patient recovered uneventfully without signs of rhabdomyolysis. The diagnosis was confirmed by serial serum creatine kinase measurements. The authors suggested that dantrolene should be made available in the operating theater of every hospital.

Keywords: Malignant hyperthermia, Desflurane, Dantrolene, Serum creatine kinase, Hypercarbia

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The incidence of malignant hyperthermia [MH] varies from 1:5,000 to 1:100,000 anesthesia with a mortality rate of 70% to 80%[1,2]. This high mortality rate was reduced to 10% after the introduction of dantrolene for the treatment of MH. Recent mortality rates are reported at less than 5% with early diagnosis using capnography and prompt use of dantrolene[2,3]. Notwithstanding, the North American MH Registry continued to report a morbidity rate of 35% between 1987 and 2006, despite the widespread use of dantrolene[4]. The authors reported a case of a female teenager diagnosed with lordoscoliosis undergoing posterior approach scoliosis surgery that developed MH during induction of anesthesia.

Case Report

A 138-cm tall, 16-year-old, female weighing 32.5 kg, diagnosed with congenital lordoscoliosis was scheduled for posterior approach scoliosis surgery. There was no family history of perioperative death. Her preoperative investigations were normal except restrictive ventilatory impairment from spirometry (forced vital capacity [FVC] = 32% of predicted value). In the operating theater, her vital signs included blood pressure 110/70 mmHg, pulse rate 90/minute, respiratory rate 20/minute, temperature 36°C, and end-tidal CO_2 [$etCO_2$] 33 mmHg. Induction of anesthesia was uneventful using fentanyl 50 µg and propofol 80 mg with cisatracurium 6 mg to facilitate intubation. Anesthesia was maintained with an O_2 0.5 L/minute + N_2O 0.5 L/minute + desflurane 6%.

Ten minutes later, the $etCO_2$ abruptly rose to 78 mmHg and was sustained despite hyperventilation. Her temperature rose to 36.8°C with a pulse rate of 158/minute. MH was suspected. The desflurane vaporizer was turned off and the patient manually hyperventilated using a self-inflating bag with 100% O_2. The anesthetic machine was replaced.

Blood gas analysis was performed and revealed both severe respiratory and metabolic acidosis, which confirmed the diagnosis (i.e., pH 7.079, pCO_2 77.2 mmHg, P/F ratio 400 mmHg, base excess -10 mmol/L, K^+ 3.7 mmol/L, and lactate 4.8 mmol/L). A blood sample was sent for measurement of serum creatine kinase [CK].

Since dantrolene was stocked in our operating theater, 80 mg dantrolene was given intravenously within 15 minutes followed by 50 mL of 8.4% sodium bicarbonate. Hyperventilation was continued. The patient's $etCO_2$ gradually decreased to 33 mmHg within 30 minutes of treatment. Her temperature was 35.8°C and her heart rate decreased to 94/minute. Another blood gas analysis was performed and revealed pH 7.374, pCO_2 42.8 mmHg, P/F ratio 500 mmHg, base excess -2 mmol/L, K^+ 3.8 mmol/L, and lactate 1.8 mmol/L. The operation was cancelled, and the patient

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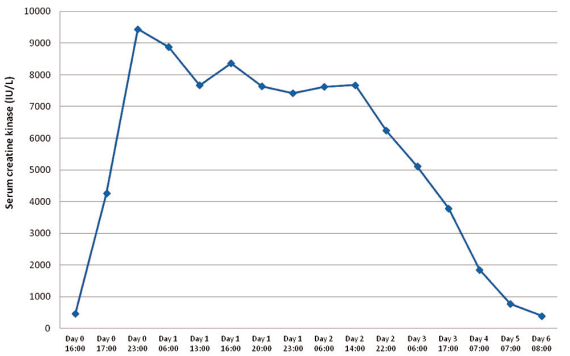

Figure 1. Serum creatine kinase level from day 0 to day 6.

was transferred to ICU. The serum CK level in the blood sample was 474 IU/L.

In the ICU, dantrolene 30 mg IV was repeated every four hours on the first day and every six hours on the second. Serial serum CK measurements were continued and revealed that CK peaked to 9,442 IU/L eight hours later and gradually decreased to 395 IU/L over the next five days (Figure 1). The patient's urine analysis, blood urea nitrogen, and creatinine values were normal throughout the admission. She was extubated on day 3 when CK level gradually decreased and all clinical symptoms were stable. She was discharged on day 7. The patient, her mother, and relatives received genetic counseling to let them know that the patient's siblings would likely be susceptible to MH, and in future they should notify the anesthesiologist that they are at risk of developing MH during anesthesia.

Discussion

MH, an autosomal-dominant inherited disease of striated muscle with mutation in the ryanodine receptor [RyR1], is a rare disorder characterized by a hypermetabolic state triggered by all inhalation anesthetics and succinylcholine[5]. Without prompt and appropriate treatment to control the crisis, hypermetabolism will be initiated, resulting in rapid consumption of energy stores and adenosine triphosphate [ATP], leading to respiratory and metabolic acidosis, followed by continuing myocyte necrosis, rhabdomyolysis, life-threatening hyperkalemia, acute renal failure, and disseminated intravascular coagulation [DIC], which could be fatal[2].

Rhabdomyolysis during MH results in a marked increase of serum CK and potassium. Serum CK measuring serves both for diagnosis and determining the severity of rhabdomyolysis[6]. Data from the North American MH Registry for patients between 1987 and 1994 showed that the respective median and peak CK values of MH patients were 1,139 and 100,000 IU/L. If the patients received succinylcholine, these values were much higher (i.e., 6,295 and 204,000 IU/L). Just as with MH patients, the CK level can also increase in non-MH patients undergoing common surgical procedures[6].

Dantrolene can inhibit this process by reacting with RyR1 receptor to impede spontaneous $Ca2^{+}$ leakage[7], so the prognosis of the patient depends on the promptness of dantrolene administration. Hence, the high morbidity rate of 35% between 1987 and 2006 reported by the North American MH Registry reflects the lack of prompt treatment in some situations despite the widespread use of dantrolene since the 1980s[4].

The most sensitive warning sign for diagnosis of MH is an abrupt rise in $etCO_2$ and tachycardia[4,8]. A progressive increase in the levels of serum CK supports the diagnosis of MH[6]. Our patient was diagnosed with MH because of the abrupt increase in $etCO_2$ and heart rate after desflurane exposure as well as severe respiratory and metabolic acidosis, which was confirmed by the pattern of serum CK.

Evidence for a definitive diagnosis includes (a) genetic testing for mutation of RYR1 gene and/or (b) the in-vitro contracture test after muscle biopsy[9]. Since our institution, like many financially constrained hospitals, has a limitation in performing both these tests, our diagnosis was based on clinical manifestations and CK levels. Our diagnosis was confirmed by the pattern of peak serum CK on the first day (rising to 9,442 IU/L without a surgical procedure) then declining toward normal after five days.

Since we had dantrolene in the operating theater, our patient was able to receive dantrolene within 15 minutes of the occurrence of symptoms. The rapid return to a normal level of $etCO_2$ and heart rate in our patient, as well as no hyperkalemia or myoglobinuria detected, confirmed that prompt treatment with dantrolene can inhibit the pathological process, so that the patient can have a very good outcome. Another factor contributing to less severe symptoms and rapid recovery in this patient was the absence of succinylcholine during the induction of anesthesia.

Limitation

Since we neither perform RYR1 gene mutation testing nor run in-vitro contracture testing after muscle biopsy, our diagnosis of MH was based solely on

clinical manifestations as well as the CK level, so the diagnosis may not be definitive.

Conclusion

Desflurane exposure in pediatric patients with congenital lordoscoliosis can trigger MH. The most sensitive warning signs are (a) a rise in $etCO_2$ and (b) tachycardia, followed by (c) an increase in temperature (hyperthermia) and (d) a sudden rise in serum CK. Prompt treatment including removal of the triggering agent and dantrolene administration can affect rapid recovery with an uneventful outcome. Dantrolene should be readily available in operating theater of every hospital.

What is already known on this topic?

Succinylcholine and inhalation anesthetics can trigger MH in MH-susceptible patients with very high mortality. Although dantrolene has been widely used since the eighties, high mortality rates persist.

What this study adds?

The authors demonstrated that prompt diagnosis and treatment with dantrolene resulted in rapid and full recovery. To achieve this goal, dantrolene should be available in every operating theater.

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Potential conflicts of interest

The authors declare no conflict of interest.

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