Letter to the Editor

PORTO BIOMEDICAL JOURNAL
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Malignant hyperthermia: a case report with good outcome

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To the Editor

We present a case report of a 63-year-old man with ocular trauma admitted to the operating room for vitrectomy. He had medical history of hypertension, dyslipidemia, alcohol abuse, and chronic obstructive pulmonary disease Gold IIIC. He had been submitted to gastric suture under general anesthesia, 30 years ago with no known complications. He denied familial history of anesthetic complications. Pulmonary wheezing and rumbles were evident at auscultation. Standard American Society of Anesthesiologists monitorization was ensured and *rapid sequence induction* with propofol, fentanyl, and rocuronium was achieved. Sevoflurane was used for maintenance. Ninety minutes after induction, $EtCO_2$ started to rise (60 mm Hg) with an obstructive capnography curve, increased airway pressure, and worsening of pulmonary wheezing at auscultation. Bronchospasm was assumed and treated with salbutamol, ipratropium bromide, hydrocortisone, magnesium sulfate, and ketamine. Despite treatment and ventilation adjustment, $EtCO_2$ continued to rise until a maximum of 100 mm Hg. An arterial blood gas (ABG) analysis was obtained, showing acidosis (pH = 7.16) with hypercapnia (pCO_2 = 88.7 mm Hg) and desaturation ($SatO_2$ = 93.9%, with FiO_2 = 60%, and pO_2 = 88.6 mm Hg). Muscular rigidity became evident and temperature increased to a maximum of 40.5°C. The diagnosis of malignant hyperthermia was assumed. Sevoflurane was discontinued. High flow ventilation (FiO_2 100%) and propofol perfusion were initiated. A dantrolene intravenous (iv) bolus (2.5 mg/kg) and 100 mL of 8.4% sodium bicarbonate were administered and active cooling measures initiated. An arterial line, central venous catheter, and urinary catheter were promptly placed. Venous blood samples were obtained to evaluate muscular enzymes, hepatic, and renal function. Intravenous crystalloids and 1 mg/kg furosemide were administered to maintain urine output and prevent renal injury. Noradrenaline infusion was started to maintain adequate median arterial pressures. ABG after starting therapeutic measures showed significant respiratory acidosis with severe hypercapnia (pH = 7.0, pCO_2 = 156.9 mm Hg), without hypoxemia (PaO_2 = 380 mm Hg with FiO_2 = 100%), and a mild increase in lactate (2.7 mmol/L). Another iv bolus of dantrolene was given (total dose of 5 mg/kg). After a few minutes, temperature and $EtCO_2$ started to drop. Forty-five minutes later, patient stabilized registering a core temperature of 37.2°C. Serialized ABG showed a progressive improvement in acidosis (pH = 7.355, pCO_2 = 67.9 mm Hg). After stabilizing, he was taken to the intensive care unit (ICU) sedated with propofol and fentanyl, intubated and with a 24-hour iv infusion of dantrolene (0.25 mg/kg/h). In the ICU, muscular and hepatic enzymes gradually normalized, and renal function remained preserved. Patient was extubated on the third day, discharged from ICU on the fourth day and from the hospital 12 days after the procedure. Patient was referenced to follow-up anesthesiology and genetic consultations, where in vitro caffeine-halothane contracture and DNA tests confirmed the diagnosis of malignant hyperthermia (MH).

Malignant hyperthermia is a rare, life-threatening and hypermetabolic response, occurring most often during general anesthesia, with an incidence estimated to be 1:100,000.[1] It is a pharmacogenetic condition affecting Ca^{2+} homeostasis in skeletal muscle, which requires an autosomal dominant genetic defect and a trigger agent like volatile anesthetics, such as sevoflurane or desflurane and depolarizing muscular blockers, such as succinylcholine.[2] Nowadays, we know MH has a definitive association with 5 congenital muscle disorders: central core disease, King-Denborought syndrome, multi/minicore disease, nemaline myopathy, and Evans myopathy.[3] Other skeletal muscle disorders causing anesthesia-induced rhabdomyolysis, which have a similar clinical presentation, do not respond to the dantrolene. Attending to the genetic basis, it is crucial to ask for history of anesthesia complications in patients or close relatives. Clinically, MH manifests as a hypermetabolic state of sustained muscle contraction with rapid increasing temperature and inappropriately CO_2 production, seen as a raised end-tidal CO_2 and tachypnea if the patient is breathing spontaneously. If not recognized and promptly treated, this hypermetabolic state can disturb acid-base balance and produce rhabdomyolysis with hyperkalemia, myoglobinuria, and, consequently, multiorgan dysfunction and death. The treatment requires immediate suspension of the trigger agent, administration of dantrolene, active cooling, and supportive measures.[4] The final diagnosis is made with in vitro contracture test.[5] DNA analysis, however, offers a noninvasive alternative to in vitro contracture test requiring only a blood specimen, and an available diagnostic laboratory.[6] It is important to be aware that clinical signs described are not specific to MH and require exclusion of other differential diagnoses which will not respond to the dantrolene.

Implication statement: Malignant hyperthermia (MH) is a rare life-threatening condition occurring with anesthesia. This clinical report describes a case of MH well identified and treated with a good outcome, highlighting the importance of early recognition and treatment.

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Porto Biomed. J. (2021) 6:1(e080)

Received: 9 April 2020 / Received in final form: 17 June 2020 / Accepted: 27 June 2020

http://dx.doi.org/10.1097/j.pbj.0000000000000080

This case report highlights that rapid recognition and treatment are essentials to improve the survival of a patient with MH. When providing his preoperative history, the patient denied any individual or family history of anesthesia complications. However, after this incident, during the follow-up anesthesiology consultation, he recognized that a first-degree cousin had a similar event with anesthesia in a routine surgery a few months before, that he did not know at the time. After genetic consultation, it was confirmed to be also a case of MH. This emphasizes the value of an accurate and complete medical and family history and the importance of patient's education on reporting their anesthesia complications and on sharing that information with close relatives. With this information, we are able to identify patients at risk and take precautionary measures to avoid MH triggers when a general anesthesia is required.

In conclusion, a good outcome in MH depends on a combination of factors. Firstly, an accurate and a complete preanesthetic evaluation is required. Secondly, the anesthesiologist needs to be aware of the pathology, correctly identify and manage it, starting administration of dantrolene as soon as possible. As this drug is the key in the treatment, an MH cart with dantrolene must be available and easily accessible in every hospital that uses trigger agents.[7]

Acknowledgments

None.

Conflicts of interest

The authors declare no conflict of interest.

References

[1] Brady JE, Sun LS, Rosenberg H, Li G. Prevalence of malignant hyperthermia due to anesthesia in New York State, 2001–2005. Anesth Analg. 2009;109:1162–1166.
[2] Cully TR, Choi RH, Bjorksten AR, Stephenson DG, Murphy RM, Launikonis BS. Junctional membrane Ca(2+) dynamics in human muscle fibers are altered by malignant hyperthermia causative RyR mutation. Proc Natl Acad Sci U S A. 2018;115:8215–8220.
[3] Litman RS, Griggs SM, Dowling JJ, Riazi S. Malignant hyperthermia susceptibility and related diseases. Anesthesiology. 2018;128: 159–167.
[4] Riazi S, Kraeva N, Hopkins PM. Updated guide for the management of malignant hyperthermia. Can J Anaesth. 2018;65:709–721.
[5] Schuster F, Müller R, Hartung E, Roewer N, Anetseder M. Inhibition of sarcoplasmic Ca2+-ATPase increases caffeine- and halothane-induced contractures in muscle bundles of malignant hyperthermia susceptible and healthy individuals. BMC Anesthesiol. 2005;5:8.
[6] Paul-Pletzer K, Yamamoto T, Bhat MB, et al. Identification of a dantrolene-binding sequence on the skeletal muscle ryanodine receptor. J Biol Chem. 2002;277:34918–34923.
[7] Ho PT, Carvalho B, Sun EC, Macario A, Riley ET. Cost-benefit analysis of maintaining a fully stocked malignant hyperthermia cart versus an initial dantrolene treatment dose for maternity units. Anesthesiology. 2018;129:249–259.