Guest Editor

Paula Foran
PhD, MACN, FACORN

Author

Catherine Kleidon
Clinical Nurse
Master of Clinical Nursing (Anaesthetics and Recovery)
MACORN, MACPAN
Cathkleidon@gmail.com

Malignant hyperthermia in a regional facility: A case study

Abstract

Malignant hyperthermia (MH) is a rare hypermetabolic state that may be triggered by both anaesthesia and non-anaesthesia triggers. The main anaesthesia triggers for MH are the depolarising muscle relaxant suxamethonium and volatile anaesthetic gases. MH presents in several ways with not all clinical symptoms being required to make a diagnosis. Safe and efficient patient management of MH requires knowledge and understanding of this inherited disorder. The perioperative team need to be aware of the tasks that are required to manage this emergency. This case study will discuss a suspected episode of MH presenting in a patient late on Christmas Eve 2018 in a regional facility. Access to the reversal drug dantrolene provided an additional challenge. The increase in knowledge gained by nursing staff involved in the management of this crisis proved to be a significant learning curve for all involved. It is hoped that this paper will enable other perioperative nurses to benefit from this experience.

Keywords: malignant hyperthermia, anaesthetic, regional facility, dantrolene, nursing management

Background

Malignant hyperthermia may be defined as a hypermetabolic state triggered under general anaesthetic by volatile anaesthetic gases and the depolarising muscle relaxant suxamethonium[1]. These drugs trigger uncontrolled levels of intracellular calcium released from the sarcoplasmic reticulum within muscle cells in the susceptible person[2]. Persistent muscle contraction results in body rigidity, raised core temperature and increased cellular oxygen demand and thus carbon dioxide production[3]. If not treated quickly and effectively, cell death, organ failure, brain injury or cardiac arrest may result[4]. Many perioperative nurses will never experience an episode of MH as it occurs infrequently[y5]. MH is triggered by specific drugs which are often used to undertake general anaesthesia[6]. Perioperative nurses must be familiar with the trigger agents, presenting signs and management of MH to avoid the life-threatening complications that can develop[3,7].

This suspected case study describes the presentation of the patient's journey and improvements that have been made since this episode, which took place in regional Queensland. This case study will present the challenges faced by an after-hours perioperative team with a patient undergoing an emergency laparoscopic appendicectomy in the late hours of Christmas Eve 2018.

Case presentation

The case being presented occurred during an emergency laparoscopic appendicectomy on a 32-year-old male who will be referred to as Mr M. Initially Mr M presented to his general practitioner with peri-umbilical pain and vomiting. Acute appendicitis was confirmed via computed tomography (CT) scan. Mr M was admitted to hospital and to the operating suite for emergency appendicectomy at 9.05 pm. The anaesthetist performed a thorough pre-anaesthetic assessment of the patient on arrival. Mr M denied any known drug allergies, medical history

or knowledge of rare anaesthetic reactions within his family. The patient's history involved previous surgeries including removal of wisdom teeth under general anaesthetic and yearly colonoscopies due to a familial history of Peutz Jegher's syndrome (bowel polyps). During all these procedures, no hypermetabolic reaction was observed. The patient was considered to be an otherwise healthy adult male and had given their consent for surgery and anaesthesia.

A rapid sequence induction was chosen for the patient due to a possible risk of aspiration of gastric contents. The patient was administered intravenous propofol, alfentanil and rocuronium at induction with cricoid pressure to protect the airway. Rocuronium is a non-depolarising muscle relaxant that is used for its quick onset to create optimal intubating conditions[8]. Following an uneventful induction and intubation, the inhalation anaesthetic gas desflurane was turned on and administered at six per cent for maintenance of anaesthesia. Oxycodone was titrated during the surgery for pain relief. The patient displayed no adverse reactions and the surgery was completed without any complications.

On completion of the surgery, the volatile anaesthetic agent was switched off and muscle relaxant reversal drugs neostigmine and atropine were intravenously administered. It was noted that the patient was slow to emerge from anaesthesia. During the emergence phase the patient became rigid, cyanotic, tachycardic, hypertensive and shook violently. He showed a marked increase in his end-tidal carbon dioxide (CO_2) levels from 45 to 92 mm Hg (normal end-tidal CO_2 is 35–45mm Hg). A tympanic membrane thermometer recorded the patient temperature as 40° C. Rises in end-tidal CO_2 levels, muscle rigidity and an increase in body temperature are all clinical indicators of an MH episode[9]. The anaesthetist surmised that the patient was experiencing an MH crisis as the patient symptoms matched multiple common symptoms of this rare disorder. An emergency code was called. The patient was re-anaesthetised with an intravenous infusion of propofol. The MH resource box was accessed along with the cardiac arrest trolley. Malignant Hyperthermia Group of Australia and New Zealand (MHANZ) task cards were handed out to the theatre and recovery team members.

When the emergency was called, the medical emergency team were attending another case and could not immediately assist. The theatre team followed the instructions on the MHANZ cards until further help arrived. Ice was collected from the kitchen, cold bags of fluid where accessed and the theatre temperature was decreased to help cool the patient. Hospital stocks of intravenous dantrolene were sourced and mixing of the drug commenced. The surgeon informed the patient's family of the emergency, initially by telephone. The family were in the facility during the crisis and were kept updated on the patient's condition by the surgeon while the patient was in theatre and upon transfer to the intensive care unit.

Investigations

There is no immediate investigation that could have been performed to determine if MH was the cause of the patient's clinical symptoms. The initial management of the crisis was to discontinue triggering agents and treat symptoms by administering dantrolene and lowering the patient's body temperature[10]. Genetic testing and fresh muscle biopsy can detect genetic mutations[11]. All patients who have a significant reaction should be referred for further investigation but, keeping this in mind, repeated exposure to causative factors can often trigger further episodes[12]. The availability of testing locations is a factor to be taken into consideration as there are only three locations in Australia that conduct the in-vitro contracture test[1]. If the patient needs to undergo surgery in the interim, volatile anaesthetic gases and suxamethonium will need to be avoided. Muscle biopsy testing has not yet been performed on this patient as the patient's wife gave birth to a pre-term baby early in 2019 taking priority in their understandably very busy lives.

Differential diagnosis

Anaesthetists must use their expertise and clinical knowledge to determine whether a patient's symptoms align with a diagnosis of MH[13]. During the case, equipment malfunction was ruled out as the cause of rising end-tidal CO_2 levels, as the ventilator and ventilator settings were assessed and considered fully functional. The soda lime canister was still within its holding capacity. Serotonin syndrome and neuroleptic malignant syndromes were excluded as the patient reported nil current medications. These syndromes typically present as a reaction to antidepressant and antipsychotic medications and show similar symptoms to malignant hyperthermia[2,14]. Serotonin syndrome does not present with a fever[14]. There are multiple clinical signs and symptoms of a MH event; however, not all clinical indicators need to be observed for the anaesthetist to determine a MH diagnosis[1]. If a patient has received a triggering agent and has symptoms, then MH should be considered as a differential diagnosis[2]. Immediate treatment is recommended to

avoid cell death and possible cardiac arrest[15]. Dantrolene is a safe medication when given with appropriate ventilatory support[1]. The patient subsequently displayed further episodes of fever, unstable blood pressure and muscle rigidity, requiring further doses and continual infusion of dantrolene while intubated in the intensive care unit.

Treatment

On the completion of surgery, end-tidal CO_2 levels had risen from 45 to 92 mm Hg. This was an indication that the body was experiencing increased oxygen consumption, thus increased CO_2 expulsion due to the hypermetabolic state[16]. The volatile agent had been previously turned off; therefore, the circuit was flushed with high oxygen flows and reconnected to the patient. It is not recommended to waste time changing anaesthetic machine circuits[1]. The patient was hyperventilated with 100 per cent oxygen and fresh gas flows to aid in the removal of CO_2.

Administration of dantrolene is the first line of treatment in a suspected MH event. Dantrolene is a skeletal muscle relaxant that works by disrupting the release of calcium from the sarcoplasmic reticulum of skeletal muscle cells[2]. Prompt administration of dantrolene restores levels of calcium in skeletal muscle cells and has a protective effect on excitation of neurotransmitters[17]. A total of 19 vials were intravenously administered to the patient by slow push via a peripheral line until muscle rigidity symptoms subsided. The patient's vital signs were continuously monitored and documented within the operating room. The remainder of the dantrolene vials were sent with the patient to the intensive care unit. The mixing of the dantrolene is a manually intensive task and required multiple staff to assist.

At the peak of the emergency the patient was sweating profusely. His temperature reached 40° C. Muscle rigidity causes rapid body temperature increases due to the increased cellular activity and energy consumption[16]. An indwelling bladder catheter was inserted in theatre. This was done to monitor for myoglobinuria (dark coloured urine) and ensure adequate urine output[1]. An arterial line was inserted in intensive care to allow for continual haemodynamic monitoring and blood gas sampling. Due to the high amounts of dantrolene requiring administration, a central line was inserted. Dantrolene can have a necrotic effect on peripheral access due to its high alkaline content[2]. The initial management of the patient in intensive care was to continue dantrolene infusions, aggressive management of temperature and monitor pathology for hyperkalaemia, coagulation parameters and treatment of acidosis[1].

Outcome and follow-up

The patient was transferred to the intensive care unit at 11.50 pm on Christmas Eve. He was placed on a ventilator and was closely monitored. He spent a total of five days in intensive care, three of which he remained ventilated. Sedation was managed by propofol and fentanyl infusions. Temperature was continually monitored by core and tympanic measurements. The patient suffered three recurring events of MH while in intensive care, when his symptoms were managed by further dantrolene administration. Each time the patient's temperature spiked, the patient also became tachycardic and hypertensive and his tremor returned.

Dantrolene doses were ceased on the second night in intensive care. The patient experienced no further MH symptoms and was successfully extubated the following morning. Continuous monitoring was performed as the patient was very weak from the large doses of dantrolene. The patient was discharged to the surgical ward on the fifth day and then discharged home on day seven, suffering no further symptoms of MH.

Discussion

The first documented case of malignant hyperthermia in Australia occurred in 1960[7]. It was discovered that ten out of 38 relatives of a Melbourne family had died during or following general anaesthesia[18]. A genetic sensitivity was suspected to be the cause of this disorder. By the 1990s a genetic connection was discovered linking calcium channels in ryanodine receptors of skeletal muscle (RYR1). Up to 70 per cent of MH vulnerable individuals carry a RYR1 mutation[19]. There are many mutations of this receptor with only 50 per cent of patients carrying known MH genes[20]. The severity of the reaction depends on the location of the protein mutation[21]. A patient who records an unequivocal muscle biopsy result needs to be treated as susceptible[9, 22]. It is important for clinicians to understand the significance of genetic sequencing specific to MH[10].

Mortality rates have decreased since the implementation of broader anaesthetic techniques, improved monitoring, increased awareness[10] and newer generation muscle relaxants that have fewer side effects than suxamethonium[8]. Mortality rates in the 1970s were almost 80 per cent; with the introduction of dantrolene these rates dropped to less than 15 per cent[19]. MH reactions do not always occur on the first exposure to anaesthetic drugs[23]. Some research argues that a minimum of three anaesthetics are needed to trigger an event[22]. Mr M had been exposed to sevoflurane during his dental

extraction with no adverse effects. The duration of the inhalational exposure and the concentration of gases delivered may explain why Mr M did not have a MH reaction on his first exposure[23]. This fact emphasises the unpredictable nature that MH presents to anaesthetic clinicians.

The circumstances discussed in this case study are unique as this crisis occurred in the late hours of the night on Christmas Eve in a small regional facility. There was minimal staff present, none of which had ever encountered this condition before. The symptoms the patient displayed did not become apparent until the completion of his surgery. The patient also experienced further episodes while intubated in intensive care. Recurrence of symptoms can occur in up to 20 per cent of cases[24]. Observation and monitoring intra- and post-operatively is of utmost importance as is knowing the clinical signs of an unfolding event. All staff that work within a perioperative department should be aware of the process to manage a patient displaying indications of a MH crisis[7]. Preparedness is the key to management and recovery from the effects of malignant hyperthermia.

Access to dantrolene

For many years there has been an agreement that each facility located in the region stocked 12 ampoules of dantrolene. If the need arises, then the other facilities would mobilise stock to the facility in need. Dantrolene is an expensive medication that has a short shelf life. The facility at that time stocked 12 ampoules of dantrolene. Problems began to occur when additional stocks of dantrolene were attempted to be mobilised from the other facilities. The closest facility was the day surgery hospital which was closed for the holidays. A second facility had surgical cases still being conducted. Understandably, they were only willing to send partial amounts of their stocks. The remaining hospital stated that they did not keep any stocks of dantrolene. The hospital coordinator was unaware of the importance of dantrolene and its presence in the operating theatre. MHANZ recommend that facilities do not rely on other hospitals for dantrolene stock in crisis management[11]. Since this event the hospital now stocks 36 ampoules of dantrolene.

The patient described in this case study has not been involved in any clinical trials. Genetic testing has not yet been commenced due to family commitments and distance from testing facilities.

Implications for practice

Dantrolene stocks

A direct outcome of this emergency was an increase in dantrolene stock levels. As this facility is in a regional location, the chief medical officer decided to increase stock to 36 vials. MHANZ recommend that in isolated areas 36 vials should be kept to ensure adequate stock if a crisis occurs[11].

Education

Anaesthetic emergencies often present without warning and require specialised skills to manage. Simulation, problem solving[25], teamwork[26], technical and non-technical skills[27] are all fundamental aspects of specialised education required for perioperative staff. All perioperative staff are encouraged to complete the online training package prepared by MHANZ. Expired stocks of dantrolene will be used to illustrate the technique of drawing up and administering the medication in planned training scenarios. Early treatment is the key to best patient outcome.

Anaesthetic nurse assessment skills

Pre-anaesthetic assessment of the patient is not only the role of the anaesthetist. Indicators of potential anaesthetic difficulties need to be recognised during the initial handover and assessment of the patient. The anaesthetic nurse is the first line of support to the anaesthetist as anaesthetic emergencies are generally unpredictable and unforeseen. Situational awareness and decision-making skills are non-technical abilities that anaesthetic nurses develop over time[28]. Systematic assessment of the patient is a fundamental skill that is based on clinical knowledge and fine-tuned with experience.

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References

1. Malignant Hyperthermia Australia and New Zealand (MHANZ). Malignant hyperthermia 2018 [Internet]. MHANZ, updated September 2018. Available from: malignanthyperthermia.org.au.
2. Long M, Ross J. Malignant hyperthermia. J Radiol Nurs 2017;36(3):152–157.
3. Riazi S, Brandom BW. Malignant hyperthermia – an update for perioperative nurses. ORNAC J 2015;33(4):16–26.

4. Lee MA, McGlinch EB, McGlinch MC, Capacchione JF. Malignant hyperthermia susceptibility and fitness for duty. Mil Med 2017;182(3):e1854-e7.
5. Mullins MF. Malignant hyperthermia: A review. J Perianesth Nurs 2018;33(5):582–589.
6. Larach MG, Klumpner TT, Brandom BW, Vaughn MT, Belani KG, Herlich A et al. Succinylcholine use and dantrolene availability for malignant hyperthermia treatment: Database analyses and systematic review. Anesthesiology 2019;130(1):41–54.
7. McCamish J. Malignant hyperthermia knowledge. Dissector. 2019;46(4):22–26.
8. Tran DTT, Newton EK, Mount VAH, Lee JS, Mansour C, Wells GA et al. Rocuronium vs. succinylcholine for rapid sequence intubation: A Cochrane systematic review. Anaesthesia. 2017(6):765.
9. Rosenberg H, Pollock N, Schiemann A, Bulger T, Stowell K. Malignant hyperthermia: A review. Orphanet J Rare Dis 2015;10(1):1–19.
10. Riazi S, Kraeva N, Hopkins PM. Updated guide for the management of malignant hyperthermia. Can J Anaesth 2018;65(6):709–721.
11. Malignant Hyperthermia Australia and New Zealand (MHANZ). Malignant hyperthermia resource kit 2018 [Internet]. MHANZ; 2018. Available from: malignanthyperthermia.org.au/wp-content/uploads/2018/09/MALIGNANT-HYPERTHERMIA-RESOURCE-KIT-2018-1.pdf.
12. Hopkins PM, Rüffert H, Snoeck MM, Girard T, Glahn KPE, Ellis FR et al. European Malignant Hyperthermia Group guidelines for investigation of malignant hyperthermia susceptibility. Br J Anaesth 2015;115(4):531–539.
13. Isaak RS, Stiegler MP. Review of crisis resource management (CRM) principles in the setting of intraoperative malignant hyperthermia. J Anesth 2016;30(2):298–306.
14. Bledsoe R. Serotonin syndrome on emergence. ISJNA 2019;18(1):55–58.
15. Osman B, Saba I, Watson W. A case report of suspected malignant hyperthermia: How will the diagnosis affect a patient's insurability? Case Rep Anesthesiol 2018;1–5.
16. Safety Committee of Japanese Society of Anaesthesiologists. JSA guideline for the management of malignant hyperthermia crisis 2016. J Anesth 2017;31(2):307–317.
17. Tudor RC, Amihaesei C, Folescu R, Stan CI, Zamfir CL. Assessment of dantrolene toxicity in intravenous long term administration. Romanian Journal of Functional and Clinical, Macro- and Microscopic Anatomy and Anthropology 2015;14(1):14–18.
18. Gulabani M, Gurha P, Ahmad S, Dass P. Intra-operative post-induction hyperthermia, possibly malignant hyperthermia: Anesthetic implications, challenges and management. J Anaesthesiol Clin Pharmacol 2014;30(4):555–557.
19. Hosokawa Y, Casa DJ, Rosenberg H, Capacchione JF, Sagui E, Riazi S et al. Round table on malignant hyperthermia in physically active populations: Meeting proceedings. J Athl Train 2017;52(4):377–383.
20. MacKay EJ, Wilkerson C, Kraeva N, Rosenberg H, Kennedy T. A rare genetic variant of the ryanodine receptor in a suspected malignant hyperthermia susceptible patient. J Clin Anesth 2016;33:144–146.
21. Klingler W, Heiderich S, Girard T, Gravino E, Heffron JJ, Johannsen S et al. Functional and genetic characterization of clinical malignant hyperthermia crises: A multi-centre study. Orphanet J Rare Dis 2014;9:8
22. Expect the unexpected: A case of malignant hyperthermia in a 14-year-old boy undergoing gastroscopy. Aust Med Stud J 2016;55–57.
23. Gupta PH, P. Diagnosis and management of malignant hyperthermia. British Journal of Anaesthesia. 2017;17(7):249-54.
24. Malignant Hyperthermia Association of the United States (MHAUS). MHAUS [Internet]. MHAUS 2017. [Available from: www.mhaus.org.
25. Cain CL, Riess ML, Gettrust L, Novalija J. Malignant hyperthermia crisis: Optimizing patient outcomes through simulation and interdisciplinary collaboration. AORN J 2014;99(2):300–311.
26. Phitayakorn R, Minehart RD, Hemingway MW, Pian-Smith MCM, Petrusa E. The relationship between intraoperative teamwork and management skills in patient care. Surgery 2015;158(5):1434–1440.
27. Parsons SM, Kuszajewski ML, Merritt DR, Muckler VC. High-fidelity simulation training for nurse anesthetists managing malignant hyperthermia: A quality improvement project. Clinical Simul Nurs 2019;26:72–80.
28. Rutherford JS, Flin R, Mitchell L. "They seem to be able to read your mind." An interview study to identify the cognitive non-technical skills of anaesthetic assistants. J Perioper Pract 2015;25(9):155–159.