Case Report

ANNALS OF MEDICINE & SURGERY

OPEN

Malignant hyperthermia in a paediatric patient; managed successfully without dantrolene: a case report

Sangina Ranjit, MD[a], Kalpana Kharbuja, MD[a], Ashish Shrestha, MD[a], Binod Timalsina, MD[a], Neeti Ranjitkar, MD[a], Ashlesha Chaudhary, MBBS[b,*]

Introduction: Malignant hyperthermia (MH) is a potentially life-threatening pharmacogenetic syndrome triggered by volatile anaesthetics, succinylcholine, and stress such as vigorous exercise.
Case presentation: The authors describe a case of an 8-year-old male who presented with classical symptoms of MH after induction of general anaesthesia and symptomatic treatment was done successfully due to the unavailability of Dantrolene.
Discussion: Definitive diagnosis of MH can be done based on a contracture test in fresh muscle biopsy in the presence of halothane and caffeine. In the absence of muscle biopsy and genetic testing, diagnosis for MH can be done based on MH scoring.
Conclusion: Anesthesiologists should be made aware that proper symptomatic management can also save the life of a patient. Also, strong advocacy should be done to ensure the availability of Dantrolene and further strengthen lab facilities to confirm diagnosis to facilitate diagnosis and management in the future.

Keywords: autosomal dominant, dantrolene, malignant hyperthermia, rhabdomyolysis

Introduction

Malignant hyperthermia (MH) is a potentially life-threatening pharmacogenetic syndrome triggered by volatile anaesthetics, succinylcholine, and rarely in humans to stress such as vigorous exercise[1]. The incidence of MH varies from 1:3000 to 1:100 000 with the prevalence slightly higher in males than females[1]. It has a high mortality rate of up to 80% depending upon early recognition and management MH clinically manifests as a hyperthermic reaction with the catabolic crisis[2] Clinical symptoms are hypercarbia, tachycardia, muscle rigidity, and hyperthermia[3,4] Management includes immediate discontinuation of the trigger agent with symptomatic treatment and administration of Dantrolene[1].

Despite being proven as the only specific treatment for MH, this drug is unfortunately still unavailable in Nepal. We describe a case of an eight-year-old male who presented with classical symptoms of MH after induction of general anaesthesia and was managed successfully without the use of Dantrolene. This case report has been reported in line with SCARE guidelines[5].

HIGHLIGHTS

- Malignant hyperthermia (MH) is a rare, life-threatening pharmacogenetic syndrome triggered by certain anaesthetics and stress.
- This case report presents an 8-year-old male who experienced classical symptoms of MH during induction of general anaesthesia, successfully managed without Dantrolene due to its unavailability.
- Prompt recognition, high suspicion, and immediate symptomatic treatment contributed to the successful outcome, highlighting the importance of early intervention in MH cases.

Presentation of case

Eight-year-old male with a history of fall injury diagnosed as a supracondylar fracture of the left humerus was planned for closed reduction-percutaneous pinning (CRPP) under general anaesthesia. Pre-anaesthetic assessment was done which revealed normal findings. There was no history of any adverse anaesthetic event noted in the patient's family. The patient's history, systemic examination, and laboratory investigations did not reveal any signs of illness. Airway examination was also essentially normal. The patient was kept nil per oral (NPO) for 6 h and clear liquid was allowed 2 h prior to the procedure. An intravenous line was

[a]Department of Anesthesia and Critical Care, Kathmandu University School of Medical Sciences, Dhulikhel and [b]Everest Hospital Pvt Ltd, New Baneshwor, Kathmandu, Nepal

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Everest Hospital Pvt Ltd, New Baneshwor, Kathmandu, 44600, Nepal. Tel.: +977 981 307 8654. E-mail: ashlesha04.ac@gmail.com (A. Chaudhary).

Annals of Medicine & Surgery (2024) 86:4139–4142

Received 8 August 2023; Accepted 25 February 2024

Published online 5 March 2024

http://dx.doi.org/10.1097/MS9.0000000000001899

secured with a 22 G cannula and the child was pre-medicated with glycopyrrolate 0.01 mg/kg (0.2 mg) IV and sedated with ketamine 0.5 mg/kg (10 mg) IV before bringing him to the Operating room.

At the operating room the patient was induced with propofol 2 mg/kg (40 mg), fentanyl 1 mcg/kg (20 mcg), and ketamine 0.5 mg/kg (10 mg) was administered for analgesia. Appropriate-sized I-GEL for age and weight was inserted after attaining an adequate depth of anaesthesia and secured after confirming proper placement by auscultation, visible chest rise, and with capnography. Anaesthesia was maintained with isoflurane 1.5 MAC and oxygen 60% with air on spontaneous ventilation. Analgesia was supplemented by an axillary block with 10 ml of 0.25% bupivacaine by peri-arterial approach via landmark technique. Routine monitoring was done with electrocardiogram (ECG), noninvasive blood pressure (NIBP), oxygen saturation (SPO2), end-tidal carbon dioxide (EtCO2), and oropharyngeal temperature. The initial temperature was 37°C.

After 15 min, a rise in EtCO2 was noted. After re-confirming no fault in the breathing system, ventilation was assisted to maintain EtCO2 within normal range. Despite the effort, EtCO2 rose from 60 to 100 mmHg and soon to an undetectable level. This was accompanied by a rapid rise in temperature to 43°C and progressive tachycardia. The presence of muscle rigidity on both upper and lower limbs was also noted. With high suspicion of malignant hyperthermia, an emergency was declared, and a call for help was announced. His total MH scoring was 68 with an MH rank of 6 (Tables 1 and 2).

Inj acetaminophen 15 mg/kg IV was given. The surgical procedure was stopped and immediate emergency management was started. Isoflurane was stopped and the patient was hyperventilated using a new circuit and filter through the auxiliary oxygen port. Propofol 50 mg/kg/min was started for maintenance anaesthesia. The patient was draped with an ice pack followed by intravenous administration of cold ringer lactate solution. The bladder was irrigated with cold saline via a Foley's catheter. An arterial blood line was secured and a blood sample was sent for gas analysis. During this management, ECG revealed a rate of 180 beats per min and ST depression suggesting hyperkalemia and acidosis. Inj calcium gluconate, sodium bicarbonate, and dextrose/insulin were administered. Blood gas analysis revealed PH: 6.89, PCO_2: 109.3 mmhg, PO_2: 270 mm of hg lactate: 8.5 mmol/l, HCO_3: 20 mmol/l Base excess: −15.8, Na: 143 mmol/l, K: 5.45 mmol/l). Laboratory parameters showed metabolic acidosis, hyperlactatemia, and hyperkalemia (Table 3) with raised creatinine kinase (CPK) total values.

Table 1

MH clinical grading scale score calculation

Clinical indicator	Points
Arterial $PaCO_2$ > 60 mmHg with appropriately controlled ventilation	15
PETCO2 > 55 with controlled ventilation	15
Rise in temperature > 38.8°C in perioperative period	10
Arterial blood pH <7.25	10
Inappropriate tachycardia	3
Masseter spasm shortly following succinylcholine administration	15
Total score	68

MH, malignant hyperthermia.

Table 2

MH clinical grading scale score interpretation

Clinical significance	MH rank	Description of likelihood
0	1	Almost never
3–9	2	Unlikely
10–19	3	Somewhat less than likely
20–49	4	Somewhat greater than likely
35–49	5	Very likely
50 +	6	Almost certain

MH, malignant hyperthermia.

The child soon developed hemodynamic instability requiring nor-epinephrine infusion up to 0.1 mcg/kg/min. The airway was secured with a 5.5 mm ID endotracheal tube and central venous access was secured. CPK total was sent which showed an initial value of 1355 U/l and was re-checked every 8 h.

Active cooling was stopped once the temperature dropped down to 38°C. He was transferred to the ICU, kept sedated, and paralyzed under controlled mechanical ventilation. D51/2NS was initiated as per Holliday Segar's method. His urine output was closely monitored and a volume of more than 2 mL/kg/h was ensured. This was achieved without forced alkaline diuresis.

The child gradually improved, and blood gases and hemodynamics normalized after 10–12 h. A peak CPK total of 8050 U/l was reported on the following day.

On the following day, after a successful breathing trial, the patient was extubated. Along with his hemodynamic and respiratory parameters, CPK and urine output monitoring were continued. After 3 days of ICU stay, the patient was transferred to the postoperative ward and discharged after 2 days of ward stay after normalization of CPK total. Family members were briefed about perioperative events and were counselled about the disease.

Discussion

Malignant hyperthermia is a hypermetabolic response to potent volatile anaesthetic gases (isoflurane > sevoflorane > desflorane) and depolarizing muscle relaxants[1]. Malignant hyperthermia episodes have been estimated to occur between 1:10 000 and 1:25 000[2]. The prevalence is higher in males than females and 52% of reported cases come under the paediatric age group under 15 years of age[2,3,6].

The penetrance of the inherited trait is variable and incomplete and it follows Mendelian inheritance autosomal dominant pattern[7]. It is difficult to determine phenotypic changes prior to exposure or before particular testing is carried out[7]. These syndromes occur due to the mutation in the gene that encodes the ryanodine receptor (RYR1) and CACNA1S gene[7]. RYR1 is responsible for releasing Calcium via the sarcoplasmic reticulum of muscle fibre and CACNA1S is responsible for the skeletal muscle calcium channel[7]. The gold standard for diagnosis of MH is the contracture test in a fresh muscle biopsy in the presence of halothane and caffeine[7]. Molecular testing is also used as a diagnostic measure but this is costly[7].

MH clinically manifests as hyperthermia to a marked degree, tachycardia, tachypnea, increased carbon dioxide production, increased oxygen consumption, acidosis, muscle rigidity, and rhabdomyolysis, all related to a hypermetabolic response[8]. Early detection of MH symptoms, particularly an

Table 3

Laboratory tests of the patient on presenting malignant hyperthermia

Laboratory variable	At OT table	6 h	12 h	24 h	2nd day	3rd day	4th day
Arterial pH	6.89	7.2	7.34	7.37			
PaO_2 arterial (mmHg)	270	280	193	103			
Paarterial CO_2 (mmHg)	109.3	55.5	45.7	47.3			
HCO_3 arterial (mmol/l)	20.0	20.9	23.9	26.4			
Plasma lactate (mg/dl)	8.5	5.4	2	1			
Plasma CPK (U/l)	1355	5730	5877	8049	5483	3050	1220
Plasma K (mEq/l)	5.45	4.33	3.6	4.22			

CPK, creatinine kinase.

increase in end-expired carbon dioxide, offers clinical diagnostic clues[8]. Since muscle biopsy and genetic testing are not available in Nepal our diagnosis was based on the MH scoring given by Larch *et al.*[8], for a definitive diagnostic indicator of MH in 1994.

After recognition of MH, help should be called and the surgeon should be notified. The first line of management in MH is to stop the offending agent. This can be done by turning off the vaporizer and bypassing the circle circuit which would contain a trace amount of the agent. An auxiliary common gas outlet (ACGO) or auxiliary oxygen flowmeter with a Mapelson circuit can be used for this purpose[1]. The patient should then be hyperventilated with 100% oxygen to lower EtCO2. Charcoal filters are available which help in limiting the patient's exposure to inhalational agents. Next would be active cooling by all routes available[1]. In our case the patient was draped with an ice pack, IV administration of cold ringer lactate was given and the bladder was irrigated with cold saline via Foley's catheter. Cooling measures are advised to be stopped at 38.5°C[9]. Hyperkalemia is common thus prompt detection and management of hyperkalemia should also be done[1]. Metabolic acidosis should also be corrected as per blood gas analysis[9].

Dantrolene is given in doses of 2.5 mg/kg as the initial dose and then the dose is titrated to tachycardia and hypercarbia[9]. Maximum dose recommended is 10 mg/kg[9]. The use of dantrolene could decrease mortality by up to 5%[2], but we could save this child without the drug because of the high level of suspicion, prompt detection of rising end-tidal carbon dioxide, and immediate start of the treatment based on clinical suspicion. Successful management of any crisis depends upon the swiftness of the response. Our incident took place during the busy hour of the day when many nurses and doctors could pour into the OR to help out. After initial management, close monitoring for at least 48–72 h is required as about 25% of patients may show recrudescence of the symptoms[9].

There is no available data regarding its incidence and prevalence in Nepal. There is only one case that has been reported to date and an article published regarding its incidence[10]. It has a high mortality rate if not treated timely and properly so it is of great importance to correctly diagnose MH and initiate treatment. All operating room health personnel must be made aware of the severity of this syndrome and trained to diagnose and manage it. The inclusion of an emergency kit designed for malignant hyperthermia management in the crash cart could be useful[7].

Conclusion

Despite its rare incidence, malignant hyperthermia is a potentially life-threatening perioperative condition that requires prompt diagnosis and treatment. Anesthesiologists should be made aware that proper symptomatic management can also save the life of a patient. Also, strong advocacy should be done to ensure the availability of Dantrolene and further strengthen lab facilities to confirm diagnosis to facilitate diagnosis and management in the future.

Ethical approval

Patient anonymity is maintained throughout this manuscript, and consent was obtained for publication from the patient.

Patient consent

Written informed consent was obtained from the patient's parent for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Source of funding

Not applicable.

Author contribution

S.R.: concept, manuscript edit and review, and guarantor. K.K.: manuscript preparation, edit and review. A.S.: manuscript preparation, edit and review. B.T.: data collection, obtaining consent from the patient, manuscript review. N.R.: manuscript preparation, edit and review. A.C.: manuscript preparation, edit and review.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Sangina Ranjit.

Data availability statement

Data sharing is not applicable to this article.

Provenance and peer review

Not commissioned, externally peer-reviewed.

References

[1] Gupta PK, Hopkins PM. Diagnosis and management of malignant hyperthermia. BJA Educ 2017;17:249–54.
[2] Almeida CG de, Colleti Junior J. Malignant hyperthermia in a child after magnetic resonance imaging: a case report. Rev Paul Pediatr 2020;38: e2018267.
[3] Rosenberg H, Davis M, James D, *et al*. Malignant hyperthermia. Orphanet J Rare Dis 2007;2:21.
[4] Saha D, Chaudhuri A, Maulik SG, *et al*. Difficulties in management of malignant hyperthermia in a rural set up of a developing country. Med J Dr DY Patil Univ 2014;7:381.
[5] Sohrabi C, Mathew G, Maria N, *et al*. The SCARE 2023 guideline: updating consensus Surgical CAse REport (SCARE) guidelines. Int J Surg Lond Engl 2023;109:1136.
[6] Glahn KPE, Ellis FR, Halsall PJ, *et al*. Recognizing and managing a malignant hyperthermia crisis: guidelines from the European Malignant Hyperthermia Group. Br J Anaesth 2010;105:417–20.
[7] Lee YC, Woo NS. Malignant hyperthermia syndrome—a case report. Korean J Anesthesiol, 21:1007–10.
[8] Larach MG, Localio AR, Allen GC, *et al*. A clinical grading scale to predict malignant hyperthermia susceptibility. Anesthesiology 1994;80: 771–9.
[9] Watt S, McAllister RK. Malignant Hyperthermia. StatPearls Publishing; 2023.
[10] Gurung PK, Bhattarai B. High index of suspicion of malignant hyperthermia: a case report. Int Res J Multidiscipl Scope 2022;03: 14–7.