ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 03 | March - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A RARE CASE ON MALIGNANT HYPERTHERMIA

Pharmaceutical Science

Ashique E P Critical care Clinical Pharmacist, IQRAA International Hospital and Research Centre, Calicut, India.

Sulfath T S Research Assistant, Calicut, India.

Dr. Faris Hussain K N Deputy Chief, Critical Care Medicine. IQRAA International Hospital and Research Centre, Calicut, India.

Likhitha Prakash* Pharm D Intern, Department of Pharmacy Practice, Srinivas College of Pharmacy, Mangalore, India. *Corresponding Author

ABSTRACT

We encountered a case of Malignant Hyperthermia (MH), an autosomal dominantly inherited disorder characterised by skeletal muscle hypermetabolism following the exposure of isoflurane. Clinical signs and symptoms during the crisis were characterized by tachycardia, hypercapnia, arrhythmia, muscular contracture, cyanosis, metabolic and respiratory acidosis, lactic acidosis, hyperthermia, coagulopathy and rhabdomyolysis. Further, based on the criteria used in Clinical Grading Scale for Malignant Hyperthermia the patient was diagnosed with Malignant hyperthermia. The patient was then treated symptomatically. Unfortunately, due to the unavailability of the drug dantrolene in our hospital the patient could not be saved. In conclusion, the good outcome in patients with MH mainly depend on factors like, complete preanesthetic evaluation, early detection and diagnosis and availability of dantrolene. As dantrolene is the key drug, it must be made available at many more hospitals so that these patients could have the best chance of survival.

KEYWORDS

Case report, Malignant Hyperthermia, Dantrolene

INTRODUCTION

Malignant hyperthermia (MH) is a rare, but life-threatening, autosomal-dominant inherited pharmacogenetic disorder that may lead to metabolic crisis of skeletal muscle in susceptible individuals following exposure to triggering agents, such as volatile anaesthetics such as halothane, sevoflurane, desflurane, the depolarizing muscle relaxant succinylcholine, and rarely, in humans, to stress such as vigorous exercise and heat.[1] MH may be considered rare, moreover it is remarkably lethal if left untreated.[2]

The incidence of malignant hyperthermia during general anaesthesia is estimated to range from 1:5000 to1:50,000-1,00,000. Mortality rate without specific treatment is 80% and decreases to 5% with the use of dantrolene sodium.[3,8] Most of the patients who are MH susceptible have no phenotypic changes without anaesthesia, it is impossible to diagnose susceptibility without either the exposure to the "trigger" anaesthetics or by specific diagnostic testing.[4] The gold standard for diagnosing MH involves a caffeine-halothane contracture test (CHCT) on a live muscle biopsy sample, but certain clinical diagnostic criteria, laboratory results, and genetic tests may also provide evidence of the diagnosis. In India, there is no centre where in vitro halothane caffeine contraction test is performed to confirm diagnosis in suspected cases.[5] Altered calcium release channels cause dysfunction of intracellular calcium homeostasis and uncontrolled calcium release from the sarcoplasmic reticulum, which may lead rapidly to a fatal hypermetabolic state known as MH crisis.[6]

Dantrolene, the drug of choice for malignant hyperthermia is a hydantoin derivative, acts as a specific ryano-dine receptor antagonist and inhibits release of calcium from sarcoplasmic reticulum without improving its reuptake. Immediate administration of dantrolene 2.5mg/kg repeated every 5minutes until cardiac and respiratory systems are stabilised is recommended. Studies in different populations have indicated that early dantrolene administration drastically reduces the incidence of complications. They revealed that the complication rates increase with delay in administration of dantrolene treatment.[7]

Case Report

A 27-year-old male was admitted to the hospital with history of road traffic accident on 25-09-22. He had complaints of pain, swelling and deformity over left shoulder. He had no known comorbidities. On physical examination he was conscious and oriented with stable vitals and Glasgow coma scale(GCS). Systemic examination showed swelling, tenderness and range of motion was painful in the left shoulder. Computed tomography imaging of left shoulder joint suggested left humerus comminuted intra articular displaced (three part) fracture. Hence, planned for open reduction and internal fixation (ORIF) left proximal humerus on 28-09-22.

During pre-surgical assessment he had no fresh complaints, GCS-E6M5V4 and vitals showed pulse rate of 82 beats per minute; blood pressure 110/70mmhg; chest bilaterally clear. Anesthetic induction was performed with fentanyl 100mcg + propofol 50 +30 mg and neuromuscular relaxation with atracurium 40mg. Intubated with cuffed endo-tracheal (ET) tube. Isoflurane inhalation of 1.5% was administered with nitrous oxide and oxygen.

During intraoperative period, initially tachycardia(132bpm) and an episode of desaturation was noted. He was ventilated with 100% oxygen and the saturation picked up to 100%. Further, tachycardia was persisting, then developed muscle rigidity and another episode of desaturation. His end tidal carbon-dioxide showed high value (>200), increased body temperature(103-104^{0}C) and muscle rigidity was persisting. He showed signs of metabolic acidosis with pH :7.01, HCO3: 10.3mmol/L. He also developed hyperkalemia, hypocalcemia, hyperglycemia, hyperchloremia and increased lactate levels. ECG reports suggested sinus tachycardia. Bedside ECHO reports suggested severe LV Dysfunction. Isoflurane was discontinued. He was diagnosed with Malignant Hyperthermia by using the Clinical Grading Scale for Malignant Hyperthermia. Injection calcium gluconate 10 mg, injection Bicarbonate 50+50mg, injection Hydrocortisone 100+100mg, injection magnesium sulphate 2+2mg and insulin-dextrose infusion was started.

Vasopressors like Noradrenaline infusion 30ml/hr, adrenaline infusion 30ml/hr and vasopressin infusion 30ml/hr was administered. He was shifted to MICU with vasopressors support. Dantrolene the key drug in the treatment of Malignant hyperthermia was unavailable. Even though, he was given with all supportive measures, unfortunately he developed first episode of cardiac arrest after 45 minutes of general anesthesia induction. Further, he was resuscitated aggressively and showed some recovery but, later developed second episode of cardiac arrest.

He was resuscitated again, ventilator and other supportive measures with noradrenaline and dopamine were given. He further developed intravascular coagulation, fall in hemoglobin (9.7g/dl) and platelet levels (50,000), multiorgan failure and started showing signs of bleeding. Even though after taking all supportive and resuscitative measures he showed poor prognosis and developed persistent vasoplegia. He was succumbed to death on 29-09-22.

Table – 1 Criteria Used In The Clinical Grading Scale For Malignant Hyperthermia

Clinical Finding	Manifestation
Respiratory acidosis	End-tidal CO2>55 mmHg; PaCO2>60 mm Hg
Cardiac involvement	Unexplained sinus tachycardia, ventricular tachycardia or ventricular fibrillation
Metabolic acidosis	Base deficit >8 m/Eql pH<7.25
Muscle rigidity	Generalized rigidity; severe masseter muscle rigidity
Muscle breakdown	Serum creatine kinase concentration >20,000/L units; cola colored urine; excess myoglobin in urine or serum; plasma [K+] >6 mEq/L
Temperature increase	Rapidly increasing temperature; T >38.8°C
Other	Rapid reversal of MH signs with dantrolene. Elevated resting serum creatine kinase concentration
Family history	Consistent with autosomal dominant inheritance

Table – 2 Markers Of Malignant Hyperthermia In The Present Case

Parameters	Before isoflurane administration	After isoflurane administration
Heart rate	92bpm	12:45pm – 81bpm 01:30pm – 132bpm
pH	------	12:15pm - 7.08 12:45pm - 7.04 01:30pm - 7.01
ETCO2	------	01:30pm >200mmhg
Body temperature	98.80F	01:30pm - 1040F
Lactate	------	12:15pm - 14.3mmol/L 12:45pm - 15.1mmol/L 01:30pm - 16.Immol/L
HCO3	-------	12:45pm - 14.2mmol/L 01:30pm - 10.2mmol/L
GRBS	112mg/dl	12:15pm - 157mg/dl 12:45pm - 236mg/dl 01:30pm - 343mg/dl
Haemoglobin	13.6g/dl	8.4g/dl
Platelets	2,72,000	50,000
ALT	-----	2079
ALP	-----	1911
Alkaline phosphate	-----	162
Total protients	-----	37
Albumin	-----	2.3
Globulin	------	1.4
Serum creatinine	0.8	2.3

DISCUSSION

In MH, the triggering elements (inhalation agents and the depolarizing muscle relaxant succinylcholine) may cause the calcium stores to be released from the sarcoplasmic reticulum, uncontrolled entry of calcium from the myoplasm, activation of biochemical routes related to muscle activation causing the contracture of skeletal muscles, glycogenolysis, and increased cellular metabolism, resulting in the production of heat, acidosis and increased lactate level. Dantrolene acts as an antagonist, and binds to a specific region in the ryanodine receptor 1 (RYR-1) channel reducing the uncontrolled release of intracellular calcium and should be available anywhere when general anaesthesia is performed. [14]

In our case, malignant hyperthermia was triggered by the nasal anaesthetic isoflurane which was administered prior to the surgery. The patient developed the symptoms of malignant hyperthermia after one hour of administration of isoflurane. He initially presented with tachycardia and an episode of desaturation further, progressing to muscle rigidity, metabolic acidosis, hyperkalaemia, increased body temperature. By using the grading scale of malignant hyperthermia he was diagnosed with the same.[13] He had been treated symptomatically moreover, he developed complications like intravascular coagulopathy, multiorgan failure and cardiac arrest. Unfortunately, due to the unavailability of the drug dantrolene Malignant Hyperthermia could not be reversed.

A case report by A.G Jensen suggest that malignant hyperthermia induced by isoflurane can be fatal even after the administration of dantrolene.[9] First case of malignant hyperthermia in India was reported in 2008.[15] Similar cases were reported by Pillai *et al*.[5] and Gupta *et al*. [10] who succumbed even after aggressive supportive measures.[5]

The usual dose of dantrolene in malignant hyperthermia is 2.5mg/kg. Dantrolene is available in 20mg/vial. A 70 kg person will require 175 mg which is almost 180 mg that is equal to 9 vials. Cost of each vial is nearly Rs 7,600. Therefore, minimum cost of treating a patient is Indian Rupees 68,400. The reason why administrators are hesitant to import the drug is because of cost, short shelf life(12months), import hassles, and possibility of wasting the drug and incurring loss to the hospital as the incidence of MH is rare. Licence from the Drug Controller of India to import Dantrolene can be obtained for a particular patient or for an institution. These formalities take a few days to a fortnight.

The Indian Society of Anaesthesiologists should take initiative to set up a national Malignant hyperthermia registry as case reports documented in journals are the only evidence to know the incidence and challenges in recognising and treating MH.

Limitations Of The Management Of This Case

Dantrolene, the drug of choice for malignant hyperthermia could not be used due to the unavailability of the drug in our hospital as it is not freely available in market and is stocked in only few hospitals in our country.

CONCLUSIONS

In conclusion, as the number of malignant hyperthermia cases are increasing, dantrolene the key drug in the treatment of MH should be made available and easily accessible in every hospitals that uses trigger agents.

REFERENCES:

[1] Rosenberg, H., Pollock, N., Schiemann, A., Bulger, T., Stowell, K. (2015). Malignant hyperthermia: a review. Orphanet journal of rare diseases, 10(1), 1-9.

[2] Osman, B.M., Saba, I.C., Watson, W.A. (2018) A Case Report of Suspected Malignant Hyperthermia: How Will the Diagnosis Affect a Patient's Insurability?. Case reports in anesthesiology.

[3] Schneiderbanger, D., Johannsen, S., Roewer, N., Schuster, F. (2014). Management of malignant hyperthermia: diagnosis and treatment. Therapeutics and clinical risk management. 10,355.

[4] Stowell, K., Rosenberg, H., Davis, M., James, D., Pollock N. (2007). Malignant hyperthermia. Orphanet Journal of Rare Diseases. 2, 21.

[5] Iqbal, A., Badoo, S., Naqeeb, R. (2017). A case report of suspected malignant hyperthermia where patient survived the episode. Saudi Journal of Anaesthesia. 11(2), 232.

[6] Riazi, S., Larach, M.G., Hu, C., Wijeysundera, D., Massey, C., Kraeva, N. (2014). Malignant hyperthermia in Canada: characteristics of index anesthetics in 129 malignant hyperthermia susceptible probands. Anesthesia and Analgesia. 118(2), 381-7.

[7] Riazi, S., Kraeva, N., Hopkins, P.M. (2018). Updated guide for the management of malignant hyperthermia. Canadian Journal of Anesthesia. 65(6), 709-21.

[8] Benca, J., Hogan, K. (2009). Malignant hyperthermia, coexisting disorders, and enzymopathies: risks and management options. Anesthesia & Analgesia. 109(4), 1049-53.

[9] Jensen, A.G., Bach, V., Werner, M.U., Nielsen, H.K., Jensen, M. H. (1986). A fatal case of malignant hyperthermia following isoflurane anaesthesia. Acta anaesthesiologica scandinavica. 30(4), 293-4.

[10] Gupta, D., Singh, P. K. (2012). Postoperative hyperpyrexia: Retracing malignant hyperthermia. Journal of Anaesthesiology, Clinical Pharmacology. 28(3), 405.

[11] Pepper, M.B., Njathi-Ori, C., Kinney, M. O. (2019). Don't stress: a case report of regional anesthesia as the primary anesthetic for gynecologic surgery in a patient with mitochondrial myopathy and possible malignant hyperthermia susceptibility. BMC anesthesiology. 19(1), 1-4.

[12] Pillai, V.S., Koshy, R.C., Balakrishnan, M., Ramakrishnan, R. (2015). Malignant hyperthermia in India: Time for awakening, useful facts on Dantrolene. Egyptian Journal of Anaesthesia. 31(1), 81-3.

[13] Larach, M.G., Localio, A.R., Allen, G.C., Denborough, M. A., Ellis, F. R., Gronert, G. A., Kaplan, R. F., Muldoon, S. M., Nelson, T. E., Ording, H. (1994). A clinical grading scale to predict malignant hyperthermia susceptibility. Anesthesiology. 80(4), 771-779.

[14] Ravaei, H., Yavari, M. J., Salehi, VM., Hejr, H. 2020. Isoflurane Induced Malignant Hyperthermia in a Patient with Glucose 6-Phosphate Dehydrogenase Deficiency and Growth Hormone Abuse. Case reports in anesthesiology. 1-7.

[15] Saxena, K. N., Dua, C. K. (2007). Malignant hyperthermia – a case report. Indian Journal of Anesthesia. 51(6), 534-5.