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Case report

Malignant hyperthermia in India: Time for awakening, useful facts on Dantrolene

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Abstract A 33 year old lady with no obvious reason to suspect susceptibility to malignant hyperpyrexia (MH) succumbed to this unexpected complication in spite of attempts to save her life with aggressive supportive measures. We are reporting this case of possible malignant hyperthermia probably the seventh reported case in India and second from Kerala in the last decade (Saxena and Dua, 2007; Punj et al., 2001; Gopalakrishnan et al., 2010; Jain, 2010; Ramakant and Singh, 2012; Sharma et al., 2012). This was the first ever case of MH in our institution in 25 years This emphasises the need to ensure availability of Dantrolene and MH kits, diagnostic centres with appropriate lab controls and above all high index of suspicion and heightened awareness among the anaesthesiologists of this potential albeit rare risk of MH in Indian population.

1. Introduction

A 33 year old lady with no obvious reason to suspect susceptibility to malignant hyperpyrexia (MH) succumbed to this unexpected complication in spite of attempts to save her life with aggressive supportive measures. We are reporting this case of possible malignant hyperthermia probably the seventh reported [1–6] case in India and second from Kerala in the last decade. This was the first ever case of MH in our institution in 25 years.

2. Case report

A thirty-three year old lady with breast cancer was scheduled for modified radical mastectomy. She underwent fibroadenoma excision under local anaesthesia 12 years back. She was known asthmatic on regular salbutamol inhaler and on auscultation occasional rhonchi were present over the chest. Her investigations were within normal limits. Pulmonary function test showed moderate obstruction. She was accepted for anaesthesia under nebulised bronchodilator cover.

After hospitalisation she was optimised with nebulised Duolin and Budecort. IV Deryphylline 200 mg and Hydrocortisone 100 mg were given on the morning of surgery. She was

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premedicated with Pantoprazole 40 mg and Alprazolam 0.5 mg orally on the previous night and morning of surgery. Her baseline vitals in the OT were pulse rate 82/min, blood pressure 120/80 mmHg, and saturation 99% on room air. IV Glycopyrrolate 0.2 mg, Midazolam 1 mg, Fentanyl 100 μg were given. After preoxygenation anaesthesia was induced with Ligncaine 60 mg, Propofol 100 mg and Vecuronium 6 mg, supraglottic airway Igel size 4 was inserted. Air entry bilaterally was confirmed and end tidal carbon dioxide was normal. Thereafter controlled ventilation was provided with 33% oxygen in nitrous oxide and Isoflourane1% in circle system and surgery started.

35 minutes after induction, fall in SpO_2 to 96% and rise in $ETCO_2$ to 50 mmHg were noted. Pulse rate became 120/min and blood pressure 140/96 mmHg. Since the patient was asthmatic, bronchospasm was suspected, but chest auscultation revealed good bilateral air entry. Light plane of anaesthesia was suspected and additional doses of Propofol 50 mg and Vecuronium 2 mg were given. Also fresh gas flow increased to 6 L, FiO_2 increased to 0.5, changed to open circuit, and saturation was restored to 100%.

In the next 10 min $ETCO_2$ rose to 70 mmHg in spite of slight manual hyperventilation with Bain's circuit. Igel was replaced with 7size oral endotracheal tube. Tachycardia 124/min and blood pressure 140/96 mmHg persisted. Isoflourane was cut off at this point. Surgeon was alerted to finish surgery fast. Upper limb rigidity was noted at this time and surgeon observed rigid pectoral muscle. Oral temperature recorded at this time was 106 °F. Provisionally diagnosis of malignant hyperthermia was made at this time. Cooling measures were immediately instituted. Cold saline infusion, cold compresses, cold gastric lavage through Ryle's tube and cold bladder wash started. Rigidity of lower limbs noted at the time of catheterisation and it was not possible to flex the lower limbs. ABG was done and report was combined metabolic and respiratory acidosis [ph 6.5, PO_2 115 mmHg, PCO_2 176.5., HCO_3 16.1 mmol/L, BE -23, Na 148 mEq/L, K.5.6 mEq/L]. Thyroid function test was done which was within normal limits.

Hyperventilation continued but $ETCO_2$ kept on increasing to 150 mmHg within 20 min, pulse rate 144/min and blood pressure 160/96 mmHg. Additional doses of Propofol, Metolar were given Hypermetabolic crisis due to thyroid storm was ruled out since she never had thyroid problem and TFT was normal. Aggressive cooling measures continued. Sodabicarbonate 100 mL given for acidosis correction. Surgery was finished and we decided to electively ventilate the patient. Relatives were informed of the patient's critical condition.

Dantrolene was not available in our institution as efforts to procure and stock it well in advance failed in spite of repeated requests as the drug was not available in the Indian market. Measures to outsource Dantrolene during the crisis had also failed.

Patient then developed bradycardia with heart rate dropping to 38/min not responding to Atropine (IV Atropine. 6 mg, 2 doses) and went into asystole. CPR started immediately, IV Adrenaline 1 mg two doses administered. ECG complexes appeared with sinus tachycardia at a rate of 160/min and peripheral pulses appeared, which worsened to stable ventricular tachycardia with a rate of 180/min. Amiodarone 150 mg given slow IV , rate came down to 90/min. Dopamine infusion started, but patient continued to have ventricular tachycardia not responding to cardioversion at 100 J. She went into ventricular fibrillation, defibrillation, CPR and drugs given as per 2010 AHA guidelines. There was no return of spontaneous circulation, asystole ensued, resuscitation continued but patient could not be saved.

3. Discussion

The points clinching diagnosis of Malignant Hyperthermia in our patient are [7],

1. Inappropriate rapid rise in end tidal CO_2 to threefold of initial values despite maintaining hyperventilation [7].
2. Muscle rigidity not responding to additional doses of muscle relaxant.
3. Inappropriate rise in body temperature to 106 °F not responding to cooling measures.
4. Combined respiratory and metabolic acidosis and BE -23 in ABG.
5. Thyroid storm ruled out by normal TFT values [T3 92 ng/dL, T4 8 μg/dL, TSH 3.4 mIU/mL].
6. Neurolept malignant syndrome ruled out as she was not on any antipsychotic drugs.
7. No history suggestive of pheochromocytoma.

Larasch et al. [7] described a raw scoring for patients to predict the possibility that a suspected hypermetabolic crisis occurring during anaesthesia is due to MH. Our patient had a total score of 81 points (Table 1) which has a likelyhood of almost certain MH.

We could not do any test regarding confirmation of muscle breakdown like blood CPK MB, serum myoglobin or urine myoglobin due to rapid worsening and death of the patient. The most confirmatory test for MH, caffeine halothane contracture testing [8] has to be done ideally after a period of 3 months of a hypermetabolic crisis to prevent false positive results [9]. Currently we do not have facility for such testing anywhere in India [10]. It is also necessary that the lab doing a CHCT should have a control with which the contraction has to be compared [11].

The relatives were explained of the situation and informed of chances of MH susceptibility among other family members.

In the first case report of MH in India [1] the author had raised similar concerns of non availability of Dantrolene and lab facilities for diagnosing MH. The editorial in Anaesthesiology [13] focussed on Malignant Hyperthermia in India following publishing a case report of MH in a boy from South India. The author after reviewing three previous case reports of MH

Table 1 Clinical indicators for calculating MH raw score.

Clinical indicator	Points
Generalised muscle rigidity	15
$PETCO_2$ > 55 mmHg with appropriately controlled ventilation	15
Arterial $PaCO_2$ > 65 mmHg	15
Inappropriate increase in temperature 106 °C	10
Inappropriate sinus tachycardia	3
Ventricular tachycardia/Ventricular fibrillation	3
Arterial base excess more negative than −8 mEq/L	10
Arterial pH < 7.25	10

Total score 81 points.

in India questions the common misbelief of nonsusceptibility to MH in Indian population [14,15]. Further they identified seven families of Indian origin who had MH reaction in the UKMH registry.

The mortality of MH in western world is coming down due to increased awareness among anaesthesiologists and Dantrolene [12]. We feel the urgent need of the hour is to be aware of possibility of MH in Indian population and prompt institution of treatment.

Dantrolene is a direct acting muscle relaxant available in vials of 20 mg each. It has to be reconstituted in 60 mL of warm water and given via blood set. It may cause hyperkalaemia and cardiovascular collapse. Skeletal muscle weakness (22%) and phlebitis (10%) are side effects. The usual dose is 2.5 mg/kg 13 A 70 kg person will require 175 mg which is almost 180 mg which is equal to 9 vials. Cost of each vial is Rs 12,500. Therefore minimum cost of treating a patient is Indian Rupees 112,500. The cost of saving an MH patient if it occurs once in a decade is close to Indian Rupees 12 lakhs considering the fact that each year Dantrolene is stocked and wasted. But of course human life cannot be equated with any amount of money. It comes in a packing of 12 vials. The manufacturer is UK based company. Minimum shipment is of 3 vials. Shelf life is 12 months [15].

The reason why administrators are hesitant to import the drug is because of cost, short shelf life, import hassles, and possibility of wasting the drug and incurring loss to the hospital as the incidence of MH is rare. In India Dantrolene is stocked in 2 corporate hospitals in New Delhi, Bangalore and Chennai and 2 major government hospitals in Mumbai and Kolkata and a major teaching hospital in Vellore. Technically it is difficult to borrow this drug from hospitals which have stocked it due to billing and licence issues.

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 MH registry as there could be several cases that are neither documented in journals nor notified anywhere. It is equally important to have lab facilities for conforming the diagnosis. The gold standard for diagnosing MH, the caffeine halothane contracture testing [8] needs proper laboratory standards relevant to the local population. Genetic studies are taken up only in those who test positive for contracture test. Currently a teaching institute in New Delhi from where MH was first reported is doing genetic testing for MH.

There remains an ethical question. In spite of the rarity of MH are we justified in providing anaesthetic services without stocking Dantrolene to deal with that one case occurring once in a decade knowing that MH is potentially lethal?

Conflict of interest

There is no conflict of interest.

References

[1] Saxena KN, Dua CK. Malignant hyperthermia – a case report. Indian J Anaesth 2007;51:534–5.

[2] Punj J, Bhatnagar S, saxena A. Malignant hyperthermia in the Indian subcontinent: non-availability of dantrolene – a cause for concern? Internet J Pharmacol 2001;1(1). http://dx.doi.org/10.5580/1a7.

[3] Gopalakrishnan CV, Suparna B, Arun V. A rare case of malignant hyperthermia in the Indian subcontinent. Anaesthesia 2010;65:1142–52.

[4] Jain G, Gupta SK, Tharwani S, Singh DK. Rare case of hyperthermia in aluminum phosphide poisoning. Indian J Forensic Med Toxicol 2010;4:26–7.

[5] Ramakant Gupta D, Singh PK. Postoperative hyperpyrexia: retracing malignant hyperthermia. J Anaesthesiol Clin Pharmacol 2012;28:405–6.

[6] Sharma Alok, Karnik Hemangi, Kukreja Sanjay, Jagger Kanchan. Indian J Anaesth 2012 Mar-Apr;56(2):212–3. http://dx.doi.org/10.4103/0019-5049.96327.

[7] Larach MG, Localio AR, Allen GC, et al. A clinical grading scale to predict malignant hyperthermia susceptibility. Anaesthesiology 1994;80:771–9.

[8] Hopkins PM. Malignant hyperthermia: advances in clinical management and diagnosis. Br J Anaesth 2000;85(1):118–28.

[9] European Malignant Hyperpyrexia Group. A protocol for the investigation of malignant hyperpyrexia (MH) susceptibility. Br J Anaesth 1984;56:1267–9.

[10] Gupta PK, Hopkins PM. Malignant hyperthermia in India. Anaesthesia 2010;65:1063–5. http://dx.doi.org/10.1111/j.1365-2044.2010.06532.x.

[11] Larach MG, North American Malignant Hyperthermia Group. Standardization of the caffeine halothane muscle contracture test. Anesth Analg 1989;69:511–5.

[12] Glahn1 KPE, Ellis FR, Halsall PJ, Müller CR, Snoeck MMJ, Urwyler A, et alRecognizing and managing a malignant hyperthermia crisis: guidelines from the European Malignant Hyperthermia Group. Br J Anaesth 2010;105(4):417–20. http://dx.doi.org/10.1093/bja/aeq243.

[13] Carpenter D, Robinson RL, Quinnell RJ, et al. Genetic variation in RYR1 and malignant hyperthermia phenotypes. Br J Anaesth 2009;103:538–48.

[14] Robinson RL, Hopkins PM, Carsana A, et al. Several interacting genes influence the malignant hyperthermia phenotype. Hum Genet 2003;112:217–8.

[15] Allman Keith G, Wilson Iain H, editors. Adrian O' Donnell drug formulary in Oxford handbook of anaesthesia. New York: Oxford University Press; 2006, p. 1118.