Malignant Hyperthermia

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ABSTRACT

Five cases of malignant hyperthermia (MH) are described. Two had succumbed to the crisis while three survived the ordeal without complications. The pathogenesis, clinical presentation and management are reviewed.

MH is a rare and potentially fatal complication of general anaesthesia. The incidence of MH has been reported to be 1 in 15,000 anaesthetics in children, and 1 in 50,000 in adults [1]. MH was first described by Denborough and Loyell in 1960 [2]. In May 26, 1971, the first case of MH developed in a young Bahraini undergoing routine surgery. In this paper we are reporting the first five cases of MH in the Gulf Cooperation Council States.

CASE HISTORIES

Case 1

A healthy Bahraini, 18 years old male was scheduled for excision of bony swelling in the right ear in May 26, 1971.

He was medically fit, had no previous anaesthetic history and was premedicated with atropine 0.6mg. Anaesthesia was induced with sodium thiopentone 300mg followed by suxamethonium 75mg. The trachea was intubated with an oral cuffed tube and anaesthesia maintained with 2% halothane and 60% nitrous oxide in oxygen. Pulse and B.P. were monitored. The surgery lasted for 45 minutes. At the end of the operation the patient developed tachychardia and fever. The temperature was 108°F. Malignant hyperthermia was diagnosed and treatment was initiated with 100% oxygen, I.V. fluids, cooling and intravenous administration of sodium bicarbonate. After three hours of management the temperature dropped to 96°F.

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The patient was transferred to the Intensive Care Unit (ICU) for continuous monitoring and care. One hour later the patient arrested and all measures of resuscitation failed.

Case 2

A 19 years old Pakistani male who was scheduled for left myringoplasty on December 27, 1977. Pre-anaesthetic evaluation revealed a small VSD, otherwise he was medically fit and weighed 53Kg and had no previous anaesthetic history. He was premedicated with Pethidine 50mg. Anaesthesia was induced with intravenous atropine 0.6mg and sodium methohexitone 100mg followed by 100mg suxamethonium. The patient was intubated with a cuffed orotracheal tube and the anaesthesia maintained with 1% halothane, 0.2% penthrane and 60% nitrous oxide in oxygen.

There was no return of spontaneous respiration and assisted ventilation was continued. Systolic pressure and pulse were stable at 100mg Hg and 60 beats/minute respectively. Halothane and Penthrane were discontinued, intravenous pethidine 20mg was given.

Forty five minutes after the induction, there was a sudden rise in pulse to 160 beats/m, systolic blood pressure to 200mm Hg, cyanosis, and the skin was hot, axillary temperature was 106°F. Diagnosis of malignant hyperthermia was made. The patient was ventilated with 100% oxygen and the surgery was abandoned. Intravenous fluids, bicarbonate, cortisone were given and external cooling methods were initiated.

Sixty minutes after the application of therapeutic measures the systolic blood pressure, pulse and temperature were 110mm Hg, 100/minute and 97.2°F respectively. The patient was unconscious, and was not responding to stimulus but attempted to breathe. He was transferred to ICU for continuous monitoring, mechanical ventilation and care. Pupils were not dilated and EEG showed no brain electrical activities.

The patient slowly showed signs of recovery. On the third day he was fighting the ventilator and weaned off the next day. On the seventh day he was fully conscious.

On January 14, 1978 he was discharged from the hospital completely recovered with no neurological impairment.

Two years later the surgery was performed successfully and uneventfully with regional block using lignocaine.

Case 3

A healthy 18 months old Bahraini male was scheduled for cystoscopy, circumcision and orchidopexy. He was noted to have bilateral hydronephrosis with normal function and had congenital dislocated hips. He had been anaesthetised at the age of 6 months for two minor surgical procedures, each lasted approximately 30 minutes. These anaesthetics consisted of an atropine premedication with nitrous oxide, oxygen and halothane induction and maintenance. Recovery was uneventful although, in retrospect, it was noted that on both occasions the patient developed pyrexia commencing on the day of the operation and lasting approximately three days.

He was considered anaesthetic risk on this occasion. The heart rate, body temperature, haemoglobin concentration and renal function were normal before operation. His body weight was 10.9 Kg. Fifty minutes before the induction, pethidine 10mg and atropine 0.3mg were given intramuscularly. Anaesthesia was induced with Althesin 1ml and maintained with 50% nitrous oxide in oxygen and 2% halothane using a T-piece circuit. An electrocardiograph monitor was connected and 5% dextrose drip started.

Forty five minutes after induction the trachea was intubated in order to provide better operative conditions (both testes being intra-abdominal), curare 2mg was then given, and the patient was manually ventilated with nitrous oxide: oxygen 4:4 litres/minute for the next forty minutes while orchidopexy and circumcision were carried out.

During this time his pulse rate varied from 140-160 beats/minute. This was similar to his pre-operative rate. The anaesthetic was judged to be normal in every other aspect. Body temperature was not monitored. The operative procedure lasted approximately 2 hours and at the end of this time neostigmine 0.4mg and atropine 0.2mg were given intravenously, at this point his pulse increased to 180-200 beats/minute and his skin was hot, rectal temperature was 40.6°C and axillary temperature 39°C. The patient became tachypnoeic, all limbs were rigid and he developed masseteric spasm. There was no cyanosis and it was decided to treat this as a case of malignant hyperthermia. Cooling with ice packs, and 100% oxygen was given together with sodium bicarbonate. Blood was taken for electrolytes, but no arterial blood gases were done, dantrolene was unavailable. The axillary temperature dropped over the next 45 minutes to 38°C. His tachycardia reduced to 160 beats/minute and thence to 140. At this point, the patient began to gag and he was extubated and given oxygen via a mask.

The patient was observed in the recovery room for the next 5 hours where he remained sleepy and his pulse rate stabilised at 130-150 beats/minute. His axillary body temperature ranged from 36.7°C to 38°C and he required cooling. Clear urine was voided on two occasions.

The patient remained sleepy during the subsequent 36 hours and again developed pyrexia which required treatment. He was apyrexial 48 hours later and his conscious state was normal. The serum creatinine phosphokinase level was normal. A muscle biopsy with histochemical and histological examination does not usually show abnormalities in children under the age of 5 years and hence was not performed in this case.

Case 4

A 32 year-old Indian male was scheduled for operative removal of foreign body from the left eye. He was thin-built with no cardiorespiratory, hepatic or renal disease. Preoperative medication consisted of intramuscular injection of pethidine 40mg and atropine 0.6mg. Anaesthesia was induced with thiopentone 250mg followed by suxamethonium 75mg. There was no adequate relaxation of the jaw and additional 25mg of suxamethonium was given.

The patient was intubated with a 9.0mm cuffed orotracheal tube with little difficulty. Anaesthesia was maintained with 2% halothane and 60% nitrous

oxide in oxygen with the patient breathing spontaneously. Monitoring was done by means of ECG, pulse and blood pressure measurements. Seven minutes after induction of anaesthesia the patient developed multiple ventricular ectopics followed by sinus tachycardia with rise in systolic blood pressure. Halothane was discontinued, alloferin 20mg was given and anaesthesia was maintained with 60% nitrous oxide in oxygen using Manley ventilator. Intravenous propranalol 3mg was given in an attempt to decrease the heart rate and systemic blood pressure.

At the end of the operation, the neuromuscular blockade was reversed with neostigmine 2.5mg and atropine 1.2mg. There was no adequate return of respiratory movement and excessive pressure was required to ventilate the lungs. The axillary temperature was 38.5°C and increased to 41°C over 15 minutes.

Malignant Hyperthermia was diagnosed and therapeutic measures were carried out in the form of cooling, intravenous fluids, intravenous bicarbonate, cortisone and correction of electrolyte imbalance. Dantrolene is not available at this centre.

Blood was collected for electrolytes and blood gases analysis. The arterial blood gases and electrolytes revealed the pH 6.838, pCo2 199.6mm Hg, p02 382.9mm Hg, base excess 7.9, sodium 144MEq/1., potassium 5.2MEq/1., chloride 102 MEq/1., bicarbonate 35, serum calcium 5.9MEq/1, and serum CPK was 634 IU. (The blood sample was taken after the initiation of the management).

Fifty minutes after the initiation of management, the temperature decreased to 36°C, the systolic blood pressure to 120mm Hg and the pulse to 98 beats/minute. The rigidity disappeared, spontaneous breathing started and cough reflex was present. The tube was not removed and 100% oxygen was maintained via a T-piece attachment. The patient was transferred to ICU for continuous observation and care.

The patient developed another MH crisis in the evening on the same day and all measures failed to resuscitate him.

Case 5

A 28-year-old Bahraini female went to USA in 1982 for repair of congenital cardiac defect. She developed MH during general anaesthesia which was successfully terminated.

In Toronto-Canada, MH susceptibility was confirmed by muscle contracture tests. She underwent uneventful general anaesthesia and surgery.

Whilst tracing her relatives, it was revealed that her mother is a member of Case 1 family.

DISCUSSION

MH is defined as a genetically determined membrane defect involving the sacroplasmic reticulum[4]. In the presence of triggering agents, the role of calcium in cellular metabolism is distorted. This will result in a fulminating metabolic crisis with massive heat production. The anaesthetic agents which may trigger MH include all volatile anaesthetics, suxamethonium, amida local anaesthetics, sympathomimetics and calcium salts.

The vast majority of patients susceptible to MH are usually normal in their histories, appearance and physical examination. They are commonly associated with a subclinical myopathy.

A small number of patients with certain diseases e.g. myopathies are predisposed to MH if exposed to the appropriate triggering agents [4,6].

The susceptibility to MH is inherited (autosomal dominant) and one episode within the family indicates that all members are at risk. A previous uncomplicated anaesthetic experience does not exclude developing MH during subsequent general anaesthesia.

MH most often develops during induction or recovery from anaesthesia, uncommonly may present in the recovery room. The clinical presentation of MH varies from the fulminant forms (Classic) to those with unusual presentations and mild symptomatology [7,8].

The characteristic signs of classic malignant hyperthermia include tachycardia, tachypnea, arrhythmias, cyanosis, hot skin (body temperature greater than 40°C) and skeletal muscle rigidity.

Laboratory evaluation of MH usually reveals metabolic and respiratory acidosis hypoxsaemia, hypercarbia, hyperkalaemia, hypercalcaemia, gross increase in serum creatine kinase and myoglobinuria [9].

When malignant hyperpyrexia is suspected or has developed, therapeutic measures must be initiated promptly which include :

1. Stop operation.
2. Discontinue all anaesthetic agents.
3. Change the rubber tubing on anaesthesia machine.
4. Hyperventilation with 100% oxygen.
5. Intravenous administration of
   a) 2mg/kg sodium bicarbonate.
   b) 2mg/kg dantrolene sodium 10.
6. Measures to control temperature by rapid external and internal cooling.
7. Measures to correct electrolytes imbalance (hyperkalaemia) and arrhythmias.
8. Monitor the BP, pulse, ECG, temperature, urine output and CVP.

CONCLUSION

The procedures to prevent and diagnose MH during surgery are simple, but identifying MH susceptible patients preoperatively is not. Many tests are available to diagnose the susceptibility to MH, but only muscle biopsy contracture tests are reliable. These are invasive techniques and performed only in a few centres in the world [11,12] .

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