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Malignant Hyperthermia Triggered by Cyclopropane during Cesarean Section

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Only one case has been reported of malignant hyperthermia (MH)[1] which occurred during pregnancy, although malignant hyperthermia susceptible (MHS) parturients have been managed during labor without triggering a crisis.[2,3] This clinical report describes MH occurring during cyclopropane anesthesia for cesarean section, treated successfully with dantrolene and cooling. The experience of anesthetizing the infant at six weeks of age for surgical correction of eventration of the diaphragm is described also.

REPORTS OF TWO CASES

Patient 1—The Mother. A 19-year-old primigravida was scheduled for elective cesarean section for cephalo-pelvic disproportion at 41 weeks. Five years previously she had an uneventful anesthetic for recurrent dislocation of right patella. Two years later she had anesthesia for peridontal surgery, after which she was "sore all over." Six months previously a tonsillectomy was abandoned shortly after induction of anesthesia but two weeks later the operation was carried out successfully. After the first attempt at tonsillectomy she was told she had nothing to worry about. Two months later the patient underwent uneventful anesthesia for recurrent dislocation of left patella. There was no personal medical history of serious illness and no family history of adverse reactions to anesthesia. The only abnormal physical finding in the patient was moderate bilateral pes cavus.

Magnesium trisilicate was administered 30 min before induction of anesthesia with cyclopropane. The trachea was intubated without difficulty. Anesthesia was then maintained with cyclopropane and oxygen 0.125:0.5 l/min. The baby was delivered 20 min later. The Apgar score was 4 at 1 min, and 8 at 5 min. Ergometrine, 0.25 mg, was given intravenously. A heart rate of 200 beats/min was observed in the mother 10 min after delivery. The jaws were then noted to be tightly clenched. This was considered to be due to light anesthesia and the inhaled cyclopropane concentration was increased. Ten minutes later the jaws were still clenched, as were the fingers of both hands; however, the arms and legs were flaccid. At this time buccal temperature was 37.9° C. Five minutes later the temperature was 38.2° C, the diagnosis of MH was made, and emergency therapy was commenced immediately.

Cyclopropane was discontinued, and ventilation was controlled with 100 per cent oxygen. External cooling was initiated with plastic bags of ice applied over the chest, abdomen, and legs. Ice water was given rectally and two electric fans were started and jugs of cold water repeatedly poured over the patient. The oral temperature was then 41° C and fell to 40.5° C 5 min later. At that time the soda lime cannister was too hot to touch, the indicator showed complete exhaustion and the soda lime was changed. Forty minutes after MH was diagnosed, 0.75 mg/kg (60 mg) dantrolene was given intravenously. This delay was due to the necessity of obtaining the drug from another hospital. Gross cutaneous vasoconstriction was evident at this time and systolic arterial blood pressure was 170 mmHg. Phentolamine, 5 mg, iv, was given to promote vasodilatation and external heat loss; systolic blood pressure decreased to 80 mmHg. Operative blood loss was estimated to be 1.0 l. Lactated Ringer's solution 1.0 l, sodium bicarbonate 100 mEq, and iced plasma protein solution, 1.0 l were given intravenously.

Shortly after dantrolene administration, the pH_a was 7.21; Pa_{CO_2} 54 mmHg; Pa_{O_2} 222 mmHg; bicarbonate 12 mEq/l; hemoglobin 9.3 g/dl; white cell count $24.8 \times 10^3/mm^3$; sodium 138 mEq/l; chloride 101 mEq/l; potassium 4.6 mEq/l; and total calcium 1.8 mM/l. The ECG monitor showed sinus tachycardia and no other arrhythmias were noted.

The patient was now conscious and straining. She was sedated with 20 mg papaveratum iv, in two divided doses shortly before transfer to the ICU of another hospital one hour after MH was diagnosed and all anesthetic agents had been discontinued. On arrival at the ICU her blood pressure was 120/80 mmHg, heart rate 65 beats/min and esophageal temperature 33.8° C, which rose to 36.6° C over the next three hours. She was conscious and cooperative but ventilation was still controlled. Six hours later, spontaneous ventilation ensued and the trachea was then extubated.

Two units of whole blood were transfused on the second day as the patient's hemoglobin level had decreased to 7.5 g/dl. Oral dantrolene, 100 mg initially, and then 50 mg three times a day were given for four days. A full clinical examination, including a neurologist's consultation, excluded any abnormality apart from pes cavus and corrected patellar dislocation. Electromyograph (EMG) and electrocardiograph were normal and myoglobinuria could not be detected at any time. Urinary catecholamines and thyroid function tests were normal. The creatine phosphokinase (CPK) level was 4650 IU/l on the second day and declined daily but was still 348 IU/l on the sixth postoperative day. The range for normal CPK level in our laboratory is 30-140 IU/l.

The patient was discharged on the thirteenth day after admission. She wears a Medic-Alert® bracelet stating that she has malignant hyperthermia susceptibility (MHS) and possesses a letter with full details of her condition and recommendations for management in an emergency. On investigation of her immediate relatives, the patient's father, a well-built, muscular man, was found to have an abnormal CPK level of 248 IU. The father was subsequently found to be MHS on caffeine contracture test, using boplar needles on right quadriceps muscle which

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developed 1.1 g of tension at 2 mM of caffeine (abnormal for that laboratory).

Patient 2—The Infant. When the patient presented for the six-weeks postnatal check, the infant was found to have eventration of the right hemidiaphragm. A preoperative EMG showed interference pattern consisting of high-frequency, "machine-gun" sounding activity. Individual motor units contained a high proportion (about 70–80 per cent) of polyphasic units with occasional short-duration units. There was no spontaneous activity. This EMG is strongly suggestive of a myopathic disorder. The preoperative CPK was 65 IU, within normal limits.

Full precautions were taken for the possibility of MH crisis occurring by using anesthetic equipment free of any volatile agents. Monitoring consisted of esophageal stethescope, electrocardiogram, rectal and nasopharyngeal thermistor probes, and doppler blood pressure apparatus. A water blanket and humidifier were attached but not turned on initially. Dantrolene powder, 20 mg, ready for dissolving in 60 ml water was at hand, together with other drugs.

No drugs were administered before induction of anesthesia. The child was given 1 mg *d*-tubocurarine (*d*Tc) 1 mg papaveratum iv, and then ventilation was controlled with 70 per cent nitrous oxide. The trachea was intubated without difficulty. Additional *d*Tc, 1 mg, and papaveratum, 1 mg, were given during the 2.5 hours of anesthesia. The heart rate was 140 beats/min increasing to 160 beats/min following infusion of blood. Systolic arterial blood pressure varied between 80 and 100 mmHg. Esophageal temperature during induction of anesthesia was 37° C and increased to 37.2° C and then slowly fell to 36.5° C. One hour after commencement of anesthesia, the water blanket and humidifier were turned on. At the end of the procedure residual effects of *d*Tc were not reversed and the trachea was extubated without incident 2 hours after the last dose.

The infant's recovery was uneventful and she was discharged from hospital twelve days after admission with the advice that she is presumably MHS until a caffeine contracture test could be performed later in life.

Discussion

There is only one documented case of malignant hyperthermia occurring in pregnancy.[1] There have been case reports of MHS parturients successfully managed with epidural[2] and spinal blockade.[3] Crawford[4] commented on the lack of incidence of MH reporting during pregnancy and postulated on the use of sex hormones as prophylaxis for MH crisis. The MH crisis occurring in this case is evidence that during pregnancy, MHS patients should not be regarded as less at risk.

Details of anesthetic agents used in previous anesthesia were not available preoperatively and the possibility of MH was entertained but dismissed. In retrospect, sufficient weight was not given to the history; however, it seemed prudent to avoid succinylcholine. Regional anesthesia was refused by the patient, so it was decided to use cyclopropane as the sole anesthetic. Cyclopropane was still available in the obstetric hospital at the time of this report, although the drug is now used rarely throughout the world.

Information obtained after cesarean section revealed that succinylcholine and halothane were used at the first attempted tonsillectomy and the anesthetist concerned could not pry the jaw open initially to introduce an airway and the blood pressure and pulse rate were raised. Temperature was not measured. In the subsequent anesthetics alcuronium and fentanyl were used. This case illustrates the difficulty in making a preoperative diagnosis of MHS from the patient's history alone without obtaining exact details of previous anesthetic exposure.

Cyclopropane is the most probable MH trigger in this case. It is a probable, but not conclusively proven, triggering agent in swine.[5] Cyclopropane has been administered uneventfully to a MHS patient who succumbed during a subsequent anesthetic.[6] In a study of 89 MH patients cyclopropane has been mentioned as a triggering agent.[7] However, details of anesthetic agents used concurrently were not mentioned in these cases. In our case two other drugs, magnesium trisilicate and ergometrine, were administered before MH crisis occurred, but both can be excluded as MH triggering agents. Oral magnesium trisilicate is not absorbed, and ergometrine's vasoconstrictive properties may have impaired heat loss, but its adrenergic blocking properties would modify the sympathetic response rather than trigger a MH crisis. Because cyclopropane was the sole anesthetic agent used we believe that cyclopropane alone or in combination with stress triggered MH in this patient.

Recently, a case has been reported of a man developing awake episodes of MH not associated with anesthetic triggering agents, and corrected with dantrolene.[8] In addition, MH developed in a patient after preoperative dantrolene prophylaxis and recommended anesthetic regimens were followed.[9] This supports Wingard's earlier observation[10] that stress is a possible triggering agent in humans as it is in swine. Stress has to be considered in addition to cyclopropane as a possible triggering agent in this case. However, there were at least three uneventful anesthetics where "stress" did not trigger MH in this susceptible patient.

Dantrolene may have contributed in terminating this MH crisis, but we believe the patient may have survived without it. Aggressive cooling had already lowered the temperature to below normal at the time dantrolene was administered. The rapid elimination of cyclopropane also may have contributed to the rapid reversal of MH. In retrospect, she probably had recovered spontaneously during a previous anesthetic from a MH episode. However, dantrolene may have contributed in the present episode to her smooth recovery, as the persistance of respiratory and metabolic acidosis indicated that MH was still present at the time of dantrolene administration. The possibility of intraoperative[11] and postoperative[12] recrudescence of MH was prevented by the effective use of iv and oral administration of dantrolene.

A probable case of MH has been reported in a premature neonate.[13] The youngest case of MH is in a six-

month-old child,[14] who was successfully treated with dantrolene. Because MH occurred in the mother in our case, the possibility of MHS has to be considered in the infant due to the hereditary nature of this condition. Therefore, all precautions were taken, except for the preoperative administration of dantrolene. The authors thought that, because of the muscle relaxant properties of this drug, it should be avoided in the presence of hypotonia. However, dantrolene was immediately available for intravenous use in the event of MH occurring.

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Intracranial Hypertension Following Cross-clamping of the Thoracic Aorta

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Management of intracranial pressure is of prime concern during anesthesia in a patient with closed head injury. Many intraoperative manipulations may adversely affect control of intracranial pressure. In this report, a case is described in which thoracic aorta cross-clamping resulted in a sudden increase in both arterial and intracranial pressure.

Report of a Case

An otherwise healthy 18-year-old man presented to the emergency room with multiple injuries following a motor vehicle accident. Neurologic examination revealed an unresponsive patient without localizing signs. An EMI scan showed diffuse cerebral edema. Aspiration of the abdominal cavity revealed free blood in the peritoneum. An uneventful splenectomy was performed following exploratory laporatomy. After removal of the spleen, a subarachnoid intracranial pressure monitor was inserted. Ventilation was controlled to maintain the Pa_{CO_2} in the range of 25–30 mmHg. Intravenous medications included 4 mg dexamethasone every 6 h, and 12.5 g mannitol every 6 hours. With systolic blood pressure in the ranges of 120–130, 130–140, and 140–150 mmHg, the corresponding mean intracranial pressures (ICP) were 9.3, 11.5, and 10 mmHg, respectively.

An aortogram, performed because of a widening mediastinal shadow on the chest roentgenogram, revealed dissection of the aortic arch distal to the left subclavian artery. Eight hours after the initial operation, the patient returned to the operating room where a left thoracotomy was performed. Anesthesia was maintained with intermittently administered intravenous thiamylal and inhalational enflurane. Enflurane was chosen to prevent intraoperative hypertension during one lung anesthesia. If enflurane had caused an elevation of ICP despite hyperventilation, substitution of narcotics and additional barbituates was planned; however, ICP did not increase after induction. Ventilation was controlled to maintain a Pa_{CO_2} between 25 and 30 mmHg. A Gott bypass shunt was inserted from the area of the left ventricular apex to the descending aorta. Prior to thoracic aorta cross-clamping, there were only minor fluctuations in arterial or intracranial pressures. Following cross-clamping of the aorta, the systolic blood pressure immediately increased from 100 to 130 mmHg, CVP was unchanged, while ICP increased from 18 to 32 mmHg. An intracranial pressure wave of 32 over 18 mmHg was also present. Sodium nitroprusside (SNP) was initiated to lower blood pressure in an attempt to reduce

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