OCCURRENCE OF MALIGNANT HYPERPYREXIA IN A PATIENT WITH OSTEOMALACIA IMPERFECTA

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SUMMARY

Probable malignant hyperpyrexia (MH) developed and was successfully treated in a 20-yr-old man during anaesthesia for reduction of a fractured mandible. The sister of this patient had died after an anaesthetic at the age of 14 yr, but malignant hyperpyrexia was not suspected. Subsequent enquiries revealed that the patient and his sister both had osteogenesis imperfecta. This case illustrates the infrequently reported association of malignant hyperpyrexia with osteogenesis imperfecta, and the difficulties in obtaining an adequate personal and family history of previous anaesthetics.

Malignant hyperpyrexia (MH) is an inherited condition presenting during general anaesthesia as a progressive increase in body temperature, associated with hypercapnoea, metabolic acidosis and, usually, muscle rigidity. The most commonly suspected triggering agents are halothane and suxamethonium. Estimates of its prevalence vary from 1 in 14000 in Canada (Britt and Kalow, 1970) to 1 in 200000 in the U.K. (Ellis and Halsall, 1980). The mortality in patients not known to be at risk is around 50% (Ellis and Halsall, 1980; Hall, 1980).

CASE REPORT

A 20-yr-old man presented with fractures of both angles of the mandible, requiring reduction and fixation under general anaesthesia. He was otherwise fit (apart from a very high alcohol intake) and asymptomatic. He remembered having had several lower limb fractures in childhood, but was uncertain as to whether he had received a previous general anaesthetic. He was anxious about undergoing anaesthesia because a sister had died at age 14 yr after an anaesthetic for reduction of a fracture. Both the patient and his father were certain that at the subsequent investigations her death had been attributed to an "overdose of anaesthetic", although neither the patient nor his father were aware of any occurrence of adverse reactions to anaesthetic drugs in their family and had not heard of MH. They were also not aware of the presence of any hereditary disease in the family, despite the fact that the patient and the sister that died had both had several fractures in childhood.

The patient was a well built, muscular young man, and, apart from the fractured mandible, clinical examination was unremarkable. He received benzyl penicillin i.m. and dihydrocodeine in the Casualty Department. Later, he was premedicated with hyoscine and papaveretum.

Anaesthesia

After pre-oxygenation, anaesthesia was induced with thiopentone and maintained with nitrous oxide and halothane in oxygen. Suxamethonium was administered, and a nasal endotracheal tube inserted. Prolonged fasciculation was noted following the injection of suxamethonium, but this was followed by relaxation. The patient's skin temperature did not feel abnormally high at this stage. An i.v. infusion was started, and monitoring (ECG and arterial pressure (Dinamap)) commenced. The patient was transferred to the operating table, breathing spontaneously.

Figure 1 summarizes the subsequent course of the anaesthetic. The patient was observed to be tachypnoeic and mildly hypertensive, and to have a rapid heart rate. Initially, this was thought to be the result of an inadequate depth of anaesthesia, but increasing the concentration of halothane, and the administration of small increments of fentanyl brought no improvement. The surgeons noticed poor relaxation of the jaw. The possibility of MH was discussed and, after increasing rigidity and a markedly increased skin temperature were noted, a thermometer was placed in the axilla; the temperature was 41 °C. At this point MH was diagnosed on clinical
grounds. Surgery was discontinued, the halothane vaporizer removed, and the anaesthetic circuit replaced by halothane-free tubing. Active cooling was commenced by surface ice packs, the rapid infusion of ice-cold saline, and rectal irrigation with cold fluids. Two 1 mg kg\(^{-1}\) doses of dantrolene were given, procainamide 400 mg (then discontinued), a total of 400 mmol of sodium bicarbonate, five 25-mg doses of chlorpromazine, and dexamethasone 16 mg. Temperature was monitored initially with a rectal thermistor, showing a peak value of 42 °C, and then by an oesophageal probe during the period of rectal irrigation. An intra-arterial cannula, central venous catheter, a further peripheral venous cannula and a urinary catheter were inserted. Mannitol and frusemide were given to prevent renal damage from the possible subsequent myoglobinuria. The initial assessment of acid-base balance and blood-gas tensions demonstrated (after some bicarbonate had already been given) acidaemia (pH 6.86), hypercapnoea (\(P_{\text{a}CO_2}\) 18.2 kPa), despite hyperventilation. Once the patient was stable, the surgeons rapidly applied eyelets for subsequent wiring of the fractures and the patient was transferred to the intensive care unit.

Subsequent course

The patient did well following operation. He received dantrolene 1 mg kg\(^{-1}\) at 12 and 24 h after surgery as prophylaxis against recurrence of the hyperthermia (Ellis and Halsall, 1980), but there was no evidence of subsequent increases in temperature or carbon dioxide production. Serum creatine kinase concentration in a blood sample obtained before operation was 497 i.u. litre\(^{-1}\) (normal range 10–120 i.u. litre\(^{-1}\)), although the patient had some tissue damage before surgery. Subsequent serial estimations of creatine kinase concentration showed a peak value of 7410 i.u. litre\(^{-1}\) on the 3rd day after operation. The patient had a subsequent admission under the care of the Metabolic Unit for investigation and, on this occasion his creatine kinase concentration was still increased, although serum pyrophosphatase concentration was within normal

![Fig. 1. Course of the anaesthetic.](https://academic.oup.com/bja/article-abstract/56/12/1443/242195)
limits, and a needle muscle biopsy was histologically normal. The Metabolic Unit are of the opinion that in vitro muscle biopsy testing is not of great value in patients suspected of being susceptible to MH. The patient has been referred to another centre for muscle biopsy, but has refused further investigation.

**DISCUSSION**

This case report describes the successful management of a case of probable MH.

Despite numerous attempts, the previous anaesthetic history of this patient has not been obtained. Hospital discharge summaries record: excision of a skin lesion at age 4 yr, bilateral hydrocele repair at age 5 yr, and limb fractures at the ages of 2, 4 and 6 yr, for some of which general anaesthesia was probably administered. However, as a result of hospital closure, selective microfilming of the contents of hospital records, and the absence of anaesthetic forms, no information is available as to which anaesthetic agents this patient had received previously. Delaying surgery for patients at possible risk of MH until previous anaesthetic notes are available would not have been of any benefit in this case.

Examination of the reports of the two anaesthetists involved in the sister’s case show a prolonged anaesthetic, using a mask, with airway difficulties, stridor, apnoea after small doses of fentanyl, tachycardia, and hypertension. This was followed by cyanosis, bradycardia, and irreversible cardiac arrest in the recovery room. The written report of one of the anaesthetists involved records that, soon after transfer to the recovery room, the patient was “hyperventilating” and “was also noted to be very hot and sweating profusely”.

Further enquiries have revealed that both our patient and the sister that died suffered from osteogenesis imperfecta in their childhood. At least four other members of this family are known to have this disease, and there is also a family history of cystic fibrosis, but no other anaesthetic fatalities are known.

MH is known to be associated with a variety of musculoskeletal disorders: kyphoscoliosis, ptosis, strabismus, hernias and recurrent joint dislocation (Britt and Kalow, 1970), sub-clinical myopathies and myotonia congenita (King, Denborough and Zapf, 1972), and central core disease (Frank et al., 1980). Osteogenesis imperfecta is a disease of variable severity involving bone fragility, ligamentous laxity, blue sclera, and a high incidence of inguinal herniae, and is probably inherited by an autosomal dominant gene (as is MH). Children with osteogenesis imperfecta have been reported to have metabolic defects, including increased body temperature, heart rate, respiratory rate and metabolic rate (Cropp and Myers, 1972). Additionally, people with osteogenesis imperfecta may have increased basal creatine kinase and pyrophosphate concentrations, both possibly associated with an increased risk of MH.

Several publications have mentioned the tendency of patients with osteogenesis imperfecta to develop hyperpyrexia, although not necessarily in a malignant form (Brown and Fisk, 1980; Libman, 1981; Cole et al., 1982). However, there appear to be only two actual case reports of this occurring (Solomons and Myers, 1973; De Pinna, 1978). A recent review of the surgical management of patients with osteogenesis imperfecta (Cole et al., 1982) recommends obtaining a careful personal and family anaesthetic history, preoperative measurements of serum creatine kinase and pyrophosphate concentrations (to ascertain the risk of MH), avoidance of common MH triggering agents, temperature monitoring, and provision of the necessary drugs and cooling apparatus beforehand in case MH develops.

We imagine that the proportion of patients with osteogenesis imperfecta that develop MH during general anaesthesia is small, but also recommend at least taking a particularly careful personal and family past anaesthetic history, checking of drugs and apparatus for treatment of MH before anaesthesia and temperature monitoring during and after operation.

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**REFERENCES**


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**ZUSAMMENFASSUNG**

Ein wahrscheinlicher Fall von maligner Hyperthermie trat auf und wurde erfolgreich behandelt bei einem 20jährigen Mann während Narkose zur Reposition eines frakturierten Unterkiefers. Die Schwester dieses Patienten war im Alter von 14 Jahren im Anschluss an eine Narkose gestorben; ein Verdacht auf maligne Hyperthermie war nicht geäußert worden. Späterer Nachruf ergab, dass sowohl der Patient als auch seine Schwester an Osteogenesis imperfecta litten. Dieser Fall stellt den gelegentlich beschriebenen Zusammenhang dar zwischen maligner Hyperthermie und Osteogenesis imperfecta sowie die Schwierigkeiten, eine adäquate Eigen- und Familienanamnese zu erheben.

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**RESUME**

Au cours d’une anesthésie en vue de la réduction d’une fracture de la mandibule chez un homme de 20 ans, une hyperpyrexie maligne (MH) probable est apparue et a été traitée avec success. La sœur de ce patient était morte après avoir reçu un agent anesthésique à l’âge de 14 ans, mais l’hyperpyrexie maligne n’avait pas été envisagée. Des recherches ultérieures révélèrent que le patient et sa sœur souffraient d’ostéogénèse imparfaite (OI). Ce cas illustre l’association de l’hyperpyrexie maligne et de l’ostéogénèse imparfaite dont il est rarement fait état, ainsi que les difficultés que soulève l’obtention de l’historique anesthésique préalable du patient et de sa famille.

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**OCURRENcia DE HIPERPIREXIA MALignA EN UN PATIENT CON OSTEOGENESIS IMPERFECTA**

En el curso de la anestesia para reducir una mandíbula fracturada, se desarrolló probable hiperpirexia maligna (MH) que fue tratada con éxito en un hombre de 20 años de edad. La hermana del paciente murió a los 14 años de edad después de la administración de un agente anestésico, pero no se sospechó una hiperpirexia maligna. Las investigaciones subsecuentes revelaron que tanto el paciente como su hermana padecían de osteogenesis imperfecta. Este caso ilustra la asociación de la hiperpirexia maligna con la osteogenesis imperfecta, la que no es objeto de informes frecuentes así como las dificultades en obtener la historia personal y familiar adecuada sobre la anestesia.