A previously fit 12-yr-old boy, who had no previous history of anaesthesia, underwent general anaesthesia using isoflurane for an elective circumcision. After uneventful surgery and anaesthesia, he suffered a cardiorespiratory arrest in the recovery room. Prompt oxygenation and cardiopulmonary resuscitation (CPR) were instituted. The initial serum potassium was 13 mmol litre\(^{-1}\) and prolonged CPR was required while potassium levels were reduced. Further investigation demonstrated a creatine kinase (CK) >70 000 U litre\(^{-1}\) which was consistent with a diagnosis of rhabdomyolysis. Despite requiring CPR for 1 h 45 min and a prolonged intensive care admission for multi-organ failure, the child has made an excellent recovery, including normal cognitive function. Subsequent genetic analysis has shown that the boy has previously undiagnosed Becker’s muscular dystrophy. We believe that the patient had acute rhabdomyolysis as a result of a volatile anaesthetic agent in association with an undiagnosed muscular dystrophy. In recent years, largely based on case report literature, there has been a shift in opinion as to the cause of such adverse perioperative events. What was previously thought to be malignant hyperpyrexia (MH) is now considered to be anaesthesia-induced rhabdomyolysis, an alternative and distinct reaction. The distinguishing feature of anaesthesia-induced rhabdomyolysis from MH is an acute rhabdomyolysis, without preceding hypermetabolism.

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practice for short anaesthetics in our hospital. Analgesia was established with acetaminophen 1 g and ibuprofen 400 mg orally on the ward before operation and a penile block performed by the surgical team before commencing the operation. On waking, the patient appeared to be in pain, so a further fentanyl 50 μg was administered incrementally, while the patient was monitored in theatre.

The LMA was removed in theatre at the end of the case, and the patient was transferred to the recovery room to be cared for by a trained paediatric recovery nurse. A comprehensive handover was given and the patient was breathing spontaneously with oxygen saturations of 99% on 5 litre min⁻¹ oxygen delivered by a Hudson mask, before the departure of the anaesthetic team. The first set of observations recorded by the recovery staff were: arterial pressure 130/60 mm Hg, heart rate 90 beats min⁻¹, saturations 97% on 5 litre min⁻¹ of oxygen, and temperature of 36.7°C. Oxygen saturation and heart rate were measured continuously in recovery, with arterial pressure recorded at 5 min intervals.

Approximately 10 min later, we were asked to review the patient urgently. The patient was making spontaneous respiratory effort and receiving supplemental oxygen, but had a reduced conscious level. The recovery nurse stated that he had woken up and complained that he could not move and appeared agitated, then underwent a sudden deterioration and became hypoxaemic. We supported his ventilation with oxygen 100% via a bag and mask. Electrocardiography was initiated and displayed a bradycardic sinus rhythm. I.V. atropine produced no improvement in heart rate. Central pulses became impalpable and cardiopulmonary resuscitation (CPR) was commenced, the trachea was intubated with a size 7.0 cuffed oro-tracheal tube, and the lungs were ventilated with oxygen 100%.

Resuscitation was conducted in accordance with Paediatric ALS Guidelines as published by the Resuscitation Council UK and the child received epinephrine, amiodarone, and defibrillation as appropriate. The first (venous) blood gas obtained ~20 min after cardiorespiratory arrest showed acidosis, severe hyperkalaemia, and hypocaplaemia (pH 6.85, P_ACO₂, 12.52 kPa, P_O₂, 3.65 kPa, HCO₃⁻, 19.5 mmol litre⁻¹, BE -17.9 mmol litre⁻¹, Na 128.2 mmol litre⁻¹, K 13.98 mmol litre⁻¹, Ca²⁺ 0.62 mmol litre⁻¹, and lactate 13 mmol litre⁻¹). Hyperkalaemia was treated with multiple doses of i.v. sodium bicarbonate, insulin/dextrose, calcium, and salbutamol infusions. He had brief and unsustained periods of cardiac output palpable during the arrest, but these were lost as soon as his cardiac rhythm reverted to either ventricular fibrillation, asystole, or pulseless electrical activity, for which DC cardioversion and continued CPR were performed as appropriate. Despite prolonged resuscitation, the decision was made to continue resuscitation until the hyperkalaemia could be corrected, because the CPR had been effective and uninterrupted from the outset. Regular cardiac rhythm and output were finally restored after 105 min and a systolic arterial pressure of 90 mm Hg was maintained with an epinephrine infusion. The patient’s serum potassium was 9 mmol litre⁻¹ and with his condition sufficiently stable, he was transferred to the adult intensive care unit (ICU) for continued cardiorespiratory support, venovenous haemofiltration, and active cooling.

After arrival on ICU, his serum CK level became available and was reported initially as ‘unrecordable’ by automated analysis, but after applying dilutional techniques was found to be in excess of 70 000 U litre⁻¹. A clotting screen was consistent with disseminated intravascular coagulation. As a diagnosis of malignant hyperpyrexia (MH) was considered a possibility at this time, a single dose of dantrolene 50 mg (1 mg kg⁻¹) was given. It is noteworthy that throughout the entire period of resuscitation, despite body exposure and later active cooling measures, the patient’s temperature was noted to be between 36.5°C and 37°C. After dantrolene administration, his temperature reduced to 35.5°C and serum potassium level reduced from 8.5 to 5.1 mmol litre⁻¹. Approximately 6 h after the initial cardiac arrest call, the patient began to regain consciousness and was noted to respond appropriately to verbal commands. He was haemodynamically stable without requiring inotropic support. I.V. sedation was commenced and mechanical ventilation continued, to enable him to be transferred by ambulance to the regional paediatric ICU (PICU) later the same day. The patient remained on PICU requiring multi-organ support for the following week. After tracheal extubation, there appeared to be no neurological impairment. He was transferred to a Paediatric Renal Unit and needed dialysis for a further week. When last reviewed, he had normal cognitive and renal function. He had minimal weakness in his proximal muscles, Gower’s sign was negative and his CK was slightly raised. He has received psychological input for post-traumatic stress disorder. Subsequent genetic testing (multiplex ligation-dependent probe amplification) revealed dystrophin gene deletions of exons 17–44. This is predicted to result in an in-frame shift, which is associated with Becker’s muscular dystrophy (BMD). Cardiological investigation has revealed no evidence of cardiomyopathy.

**Discussion**

This previously fit patient had a cardiac arrest in recovery after elective surgery. No succinylcholine was used and the anaesthetic, which included isoflurane, was uneventful. Cardiac arrest was diagnosed promptly and resuscitation was commenced immediately. Initially, it was not clear whether the profound hyperkalaemia was the cause of, or secondary to, the cardiac arrest, as the first blood sample was obtained 20 min after the arrest. Despite a lack of a spontaneous cardiac output for a prolonged period, resuscitation was continued while measures were taken to reduce the serum potassium level.

MH was considered to be a possible diagnosis, as it is known to occur with volatile anaesthetic agents, leading to hyperkalaemia and hypercapnia, which were evident on our initial blood gas, but there was no accompanying
pyrexia or muscle rigidity. The picture of rhabdomyolysis was supported by the CK results, which were 70 474 U litre⁻¹ post-resuscitation and 210 646 U litre⁻¹ after 7 h. Subsequent questioning revealed that the patient had met his normal motor milestones, carried out normal activities for his age, but was not particularly sporty. There was no known family history of neuromuscular disorders. Screening for an underlying neuromuscular problem was consistent with BMD.

A literature search revealed several case reports of anaesthesia-induced rhabdomyolysis which resulted in perioperative cardiac arrests in boys with BMD. Some were initially thought to be MH-like events, but these are now considered to be anaesthesia-induced rhabdomyolysis, an alternative and distinct reaction. In two cases, boys aged 6 and 18 yr, a diagnosis of BMD was known.² ³ In the two other cases, in boys aged 3 months and 3 yr, muscular dystrophy was only diagnosed subsequent to the adverse anaesthetic event.⁴ ⁵ In all but one,¹ resuscitation was successful.

The underlying pathophysiology of anaesthesia-induced rhabdomyolysis is unknown. It has been postulated that the depolarizing neuromuscular blocking agents and inhalation anaesthetic agents stress an already unstable sarcolemma causing increased permeability and its breakdown. This results in an influx of calcium and leak of intracellular potassium and CK from myocytes.⁶ As many of these reactions occur after operation, others have suggested that the causative drugs destabilize the sarcolemma in the intraoperative period, but the ultimate precipitant for rhabdomyolysis is the subsequent movement on waking. It has been suggested that anaesthesia-induced rhabdomyolysis occurs more often in younger patients with DMD and slightly older patients with BMD, as this is the time when there is the peak number of regenerating muscle fibres which are most susceptible to rhabdomyolysis.⁷–⁹

As MH was our initial working diagnosis, dantrolene (1 mg kg⁻¹) was administered in ICU and again in PICU with seemingly good effect. The use of dantrolene in similar cases of anaesthesia-induced rhabdomyolysis or MH-like episodes is controversial. In MH, it is suggested that dantrolene inhibits excessive release of calcium from the sarcoplasmatic reticulum by binding to a ryanodine receptor isoform, RYR 1,¹⁰ whereas anaesthesia-induced rhabdomyolysis seems to involve the breakdown of muscle cell membranes and then leakage of their contents. Those who suggest its continued use in these events argue that anaesthesia-induced rhabdomyolysis may share the final common pathway as MH, which can be reversed by the membrane-stabilizing effect of dantrolene.³

We believe our patient suffered a cardiac arrest in the immediate postoperative period secondary to hyperkalaemia. This is suspected to be due to rhabdomyolysis secondary to the use of volatile anaesthetic agents in association with BMD, which had not been diagnosed before his operation. It is remarkable that he has no neurological, cardiac, or renal impairment despite 105 min of cardiorespiratory arrest and a prolonged intensive care admission with multi-organ failure.

It has been suggested⁷ that short-acting i.v. agents should be used in patients with known neuromuscular disorders and that volatile anaesthetic agents should be avoided, but this is not currently universal practice. It is known that rhabdomyolysis may occur with propofol, but also that propofol has been used without adverse effects in patients with known MH. In our case, if the diagnosis of BMD had been known or suspected, a total i.v. anaesthesia or regional technique could have been used. In patients with a history suggestive of underlying muscular disease, the value of screening with a CK value taken before operation has been proposed.¹¹

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References
7 Yemen TA, McClain C. Muscular dystrophy, anaesthesia and the safety of inhalational agents revisited; again. Paediatr Anaesth 2006; 16: 105–8