An unusual case of malignant hyperthermia presenting on the acute medical take

Introduction

Malignant hyperthermia is an uncommon (incidence of 1:100 000) (Brady et al, 2009), life-threatening pharmacogenetic disorder manifesting clinically as a hypermetabolic crisis when a susceptible individual receives a halogenated inhalational anaesthetic or depolarising muscle relaxant. There has been an emergence of case reports describing a delayed onset of symptoms in malignant hyperthermia, often without the cardinal symptoms expected in fulminant malignant hyperthermia such as masseter spasm or overt hyperthermia (Evans et al, 2002; McKenney and Holman, 2002).

This case report describes a patient who was discharged home following a failed endotracheal intubation using suxamethonium and then re-admitted several hours later with severe rhabdomyolysis and an acute kidney injury. On recovery, he was referred for a muscle biopsy which confirmed an underlying genetically defined myopathy making the patient susceptible to malignant hyperthermia. This case highlights the potential for a delayed onset and wide variety of symptoms in malignant hyperthermia, enforcing the importance of vigilance not only intraoperatively but also during recovery from a general anaesthetic.

Table 1. Pre- and post-induction observations

	Pre-induction	+ 30 minutes (in recovery)
Heart rate (bpm)	82	86
Respiratory rate (bpm)	14	16
Systolic blood pressure (mmHg)	140	118
Diastolic blood pressure (mmHg)	76	68
Temperature (°C)	36.9	37.0
Oxygen saturation (%)	100	98
End tidal CO_2 (%)	4.5	5.4

Dr R Jones *is Core Medical Trainee,* **Dr F Shahid** *is Cardiology Registrar and* **Dr RPW Cowell** *is Consultant Cardiologist in the Department of Cardiology, Wrexham Maelor Hospital, Wales, L13 7TD*

Correspondence to: Dr R Jones (rhys.jones@doctors.org.uk)

Discussion

Perioperative mortality associated with hyperthermia has been reported since the introduction of general anaesthetic in the 19th century. Susceptibility to malignant hyperthermia may be acquired or inherited in an autosomal dominant fashion, with mutations to genes encoding for proteins that regulate intracellular calcium levels implicated in the pathophysiology (O'Sullivan et al, 2001).

Malignant hyperthermia is most commonly precipitated by the administration of halogenated inhalational anaesthetics such as halothane and sevoflurane or, less commonly, the depolarising muscle relaxant suxamethonium. Very rarely, malignant hyperthermia may be evoked through

Case Report

A 63-year-old man with a past medical history of hypertension, obesity and sleep apnoea was referred for an elective panendoscopy under general anaesthetic. He had a prior history of several uneventful general anaesthetics for routine operations throughout his life, including an appendicetomy as a child and several orthopaedic procedures following a road traffic collision 15 years earlier. He denied any previous adverse reactions to general anaesthetic or any family history of sudden or unexpected intraoperative death. A difficult airway was anticipated because of his increased body habitus and history of sleep apnoea, so a rapid sequence induction with video laryngoscope was opted for at the pre-anaesthetic assessment. He was induced using intravenous propofol 200 mg, suxamethonium 100 mg, ondansetron 4 mg and fentanyl 50 μg. Owing to a difficult intubation the procedure was abandoned in the anaesthetic room and the patient was returned to the recovery room for observation (*Table 1*). He made an uneventful recovery with the exception of reporting some mild diffuse muscle stiffness, but all his physiological observations were within acceptable parameters and he was discharged home.

Four hours post-discharge the patient presented to the emergency department complaining of severe muscle cramps and passing dark urine. Serum creatine kinase was significantly raised at over 42 000 IU/litre (normal range 40–230 IU/litre), and was associated with an acute kidney injury (creatinine 116 umol/litre from a normal preoperative baseline of 90 umol/litre). Arterial blood gas revealed a mixed respiratory and metabolic acidosis – FiO_2 (fraction of inspired oxygen) 28%, pH 7.23, PaO_2 = 14.2 kPa, $PaCO_2$ = 8.3 kPa, base excess -4.1 mmol/litre and bicarbonate 13 mmol/litre. He was treated with intravenous fluids and made a full recovery. Further interrogation of the history elicited similar episodes following previous general anaesthetics, where he reported much less severe generalized muscle aches postoperatively. Consequently, the patient was referred to a specialist malignant hyperthermia investigation unit for further testing.

At this point a muscle biopsy was undertaken, with in-vitro static and dynamic tests demonstrating a sustained contracture of greater than 0.2 g with 1% halothane and 2.0 mM of caffeine, confirming that the patient had an increased susceptibility to malignant hyperthermia. This was supported by the histopathology report, which demonstrated a mild increase in fibre diameters as a result of occasional atrophic type 1 fibres. Furthermore, oxidative enzyme staining showed two fibres with rimmed vacuoles in keeping with a diagnosis of central core disease. The patient was informed of the diagnosis and the panendoscopy was re-scheduled without the use of suxamethonium or halogenated inhalational anaesthetics which proceeded without any complications.

biological stresses including exercise and heat exhaustion (Jungbluth, 2007).

As demonstrated in this case report, the onset of clinical presentation in malignant hyperthermia is variable and several case reports have described a delayed onset of malignant hyperthermia postoperatively (Evans et al, 2002; McKenney and Holman, 2002). The mechanism behind the variability in the interval between drug administration and presentation onset is not fully understood and is suspected to be multifactorial (Visoiu et al, 2014).

Cardinal signs of malignant hyperthermia include masseter spasm, tachycardia and an unexpected rise in end-tidal carbon dioxide despite increased minute ventilation. Core temperature may rise above 40°C, but it is important to note that normothermia does not exclude the diagnosis, such as in this case report, and that hyperthermia is a delayed rather than immediate effect of the body's failure to autoregulate its core temperature. Similarly, false reassurance must not be sought in a patient with a prior history of uneventful general anaesthetics, as was also observed in this case report. Interestingly, one review cites that the average malignant hyperthermia patient will have had three uneventful general anaesthetics before having a documented reaction (Rosenberg et al, 2007).

Survival rates from malignant hyperthermia have improved significantly since the introduction of dantrolene, from greater than 80% mortality in 1970 to 1.4% in 2006 (Larach et al, 2008). Once a clinical diagnosis has been established and the patient has recovered, he/she should be referred for further investigation to ascertain if there is an underlying myopathy such as central core disease making the patient (and potentially all first-degree relatives) susceptible to malignant hyperthermia. In all likelihood the incidence of malignant hyperthermia is under-reported as a result of the subclinical picture of some patients and the potential for delayed onset of symptoms such as in this case report. **BJHM**

Brady JE, Sun LS, Rosenberg H, Li G (2009) Prevalence of malignant hyperthermia in New York State, 2001-5. *Anesth Analg* **109**: 1162–6 (doi: 10.1213/ane.0b013e3181ac1548)

Evans TJ, Parent CM, McGunigal MP (2002) Atypical presentation of malignant hyperthermia. *Anesthesiology* **97**: 507–8 (doi: 10.1097/00000542-200208000-00032)

Jungbluth H (2007) Central core disease. *Orphanet J Rare Dis* **2**: 25–30 (doi: 10.1186/1750-1172-2-25)

Larach MG, Brandom BW, Allen GC et al (2008) Cardiac arrests and deaths associated with malignant hyperthermia in north America from 1987 to 2006: a report from the north American malignant hyperthermia registry of the malignant hyperthermia association of the United States. *Anesthesiology* **108**: 603–11 (doi: 10.1097/aln.0b013e318167aee2)

McKenney KA, Holman SJ (2002) Delayed postoperative rhabdomyolysis in a patient subsequently diagnosed as malignant hyperthermia susceptible. *Anesthesiology* **96**: 764–5 (doi: 10.1097/00000542-200203000-00038)

O'Sullivan GH, McIntosh JM, Heffron JJ (2001) Abnormal uptake and release of Ca2+ ions from human malignant hyperthermia-susceptible sarcoplasmic reticulum. *Biochem Pharmacol* **61**: 1479–85 (doi: 10.1016/s0006-2952(01)00604-9)

Rosenberg H, Davis M, James D et al (2007) Malignant hyperthermia. *Orphanet J Rare Dis* **2**: 21 (doi: 10.1186/1750-1172-2-21)

Visoiu M, Young MC, Wieland K, Brandom BW (2014) Anesthetic drugs and onset of malignant hyperthermia. *Anaesth Analg* **118**: 388–96 (doi: 10.1213/ane.0000000000000062)

LEARNING POINTS

- Malignant hyperthermia can present at any point from administration of the trigger agent until several hours post-anaesthetic.
- Symptoms can be variable, and both normothermia and a prior history of uneventful general anaesthetics may provide false reassurance if a high index of suspicion is not maintained. Early recognition and prompt action are key.
- Failure to recognize subtle physiological and clinical abnormalities may lead to premature discharge of patients who would otherwise require close inpatient observation and possible life-saving intervention.
- Both anaesthetic specialists and hospital physicians need to be aware of this presentation, as these patients may be referred onto a general medical take after discharge from an elective day case theatre list hours or days earlier.