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Malignant hyperthermia crisis in a 14-year-old boy – a case report

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Dear Editor,

We have read the article by Cieniewicz *et al*. [1] concerning malignant hyperthermia (MH) with great interest. The disorder is very rare, so although anaesthesiologists are expected to learn about it, very few have encountered it in practice. To highlight the fact that MH is not just a theoretical issue and can occur unpredictably, we would like to present a case of a 14-year-old boy, who developed the MH crisis during general anaesthesia for testicle torsion surgery.

A 14-year-old boy with a history of uncomplicated anaesthesia for adenotonsillotomy was admitted to a paediatric hospital with symptoms of left testicle torsion. After admission, he was qualified for emergency surgery. As he had just eaten breakfast, the anaesthesiologist decided to perform general anaesthesia with rapid sequence induction. Propofol 100 mg, fentanyl 50 µg and suxamethonium 100 mg were administered and the patient was successfully intubated. The anaesthesia was provided with sevoflurane 1.5 MAC, additional boluses of fentanyl, and atracurium. The vital parameters were stable for the first 30 minutes of anaesthesia: HR 76–84 min^{-1}, SpO_2 97–100%, BP 95/45–110/60 mmHg, $etCO_2$ 48–50 mmHg, temperature 36.5°C. Towards the end of the surgery, increasing tachycardia up to 160 min^{-1} occurred with a concurrent drop in blood pressure to 75/35 mmHg. Then, a sudden rise of et CO_2 to 100 mmHg was noted, along with a rise in temperature to 39.9°C. Arterial blood gas analysis revealed acidosis with pH 7.11, pCO_2 95 mmHg, pO_2 170 mmHg, blood lactate 2.5 mmol L^{-1} and potassium level 7 mmol L^{-1}. MH was diagnosed. The sevoflurane was replaced by propofol infusion and ventilator settings were corrected to increase the ventilation; the anaesthetic machine was replaced with a ventilator. Dantrolene 2.5 mg kg^{-1} was administered intravenously. Dopamine infusion was necessary to maintain adequate blood pressure. Physical cooling (ice pads) and infusion of cold saline were started as well. Soon after the administration of dantrolene, HR started to stabilise and in 30 minutes $etCO_2$ dropped to about 48 mmHg and temperature to 36.6°C. Meanwhile the surgery was finished. The boy was sedated with propofol infusion and transferred to the ICU. The dynamics of serial ABG results are shown in Table 1.

On admission, his vital parameters were as follows: HR 110 min^{-1}, SpO_2 100%, temperature 36.6°C, BP 100/55 mmHg. First dopamine and noradrenaline infusion and fluids were necessary to maintain blood pressure but quickly stabilization was achieved. Sedation was withdrawn and the boy was extubated 2 hours after surgery. Hyperkalaemia quickly resolved. Urine was reddish, suggesting myoglobinuria, so diuresis was forced by intravenous fluids and furosemide. Serum creatinine, creatinine kinase and CK-MB were elevated. Results of laboratory tests are shown in Table 2. Echocardiography was normal.

On the third postoperative day the patient was transferred to the Department of Paediatric Surgery and four days later discharged home. At discharge, the patient's mother was thoroughly informed about the essence of the disease and potential risk

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for family members. The patient was offered a possibility of genetic testing within a scientific programme. The test revealed the mutation of the RyR 1 gene, variant NM_001042723:c.12685G>C in exon _90/105. Ever since the incident, the boy has carried a bracelet informing about his susceptibility to MH. Unfortunately, free diagnostics was possible only for him, and the family members have not been tested.

MH is a potentially fatal genetic disorder affecting myoplasmic calcium homeostasis. In the majority of cases, the mutation involves ryanodine receptor 1 (RyR1) on chromosome 19. Due to the genetic defect, exposure to volatile anaesthetic gases or depolarizing muscle relaxants leads to uncontrolled rise of myoplasmic calcium leading to a hypermetabolic response [2]. The extensive rise of intracellular calcium leads to abnormal skeletal muscle metabolism causing activation of muscle contraction, increased oxygen consumption and CO_2 production. Massive ATP hydrolysis occurs due to enhancement of intracellular mechanisms of channel pumps (Ca^{2+} pumps) for restoration of normal calcium concentration [3, 4]. Excessive heat production occurs, and the declining levels of ATP cause the destruction of membrane integrity and release of potassium and creatinine kinase. Rapid consumption of energy stores leads to mixed acidosis and lactates accumulation. Myocyte death, rhabdomyolysis and myoglobinuria may lead to kidney injury. Severe hyperthermia may cause multiorgan dysfunction and disseminated intravascular coagulation [2]. The incidence of MH is very low, between 1 : 10 000 and 1: 250 000 anaesthetics [5, 6]. MH episodes develop more frequently in males and 52.1% occur in children under 15 years old [5, 6]. Some disorders such as central core disease, centronuclear myopathy, and King-Denborough syndrome are associated with MH, but often the patients do not present accompanying symptoms [2]. In addition, the history of uncomplicated anaesthesia does not mean that the patient is not at risk; up to 13.2% of patients require three anaesthetics before triggering [7].

TABLE 1. Arterial blood gas results

Parameter	At diagnosis	After dantrolene	1 hour later	2 hours later	4 hours later
pH	7.11	7.29	7.39	7.34	7.37
pCO_2 (mmHg)	95.0	53.0	32.6	41.4	40.1
pO_2 (mmHg)	140	460	450	171	91
BE	−8.0	−6.5	−5.3	−3.1	−2.7
Lactate (mmol L^{-1})	2.5	1.9	1.8	0.9	1.0
Potassium (mmol L^{-1})	7.0	6.2	5.7	3.4	3.2

BE – base excess

TABLE 2. Daily laboratory test results

Day	Serum creatinine	CK	CK-MB mass
Reference values	0.2–0.7 mg dL^{-1}	33–145 U L^{-1}	< 5.1 ng L^{-1}
1 (surgery)	1.5	5496	34.89
2	0.9	104 605	287.04
3	0.8	95 548	94.85
4	0.7	83 319	25.29
5	0.7	66 112	14.46
6		36 524	10.70
7		17 389	5.92
8		2112	4.86
9		1026	
10		660	
11		474	

The pathophysiology, symptoms and diagnostics of MH were recently widely reviewed by Cieniewicz *et al.* [1]. The earliest symptoms are the masseter spasm, tachycardia, and hypercapnia. Hyperthermia, sometimes up to 44°C, is present only in 60% of cases. A Clinical Grading Scale for Malignant Hyperthermia was proposed by Larach *et al.* [8]. The scale uses six assessment criteria: presence of muscle rigidity (generalized or masseter spasm), signs of muscle breakdown (elevation of serum CK, red colour of urine, myoglobin in urine, hyperkalaemia), respiratory acidosis (hypercarbia, tachypnoea), inappropriate temperature increase and cardiac involvement (arrhythmia, tachycardia). According to the scale, our patient's score was 63, which makes the diagnosis "almost certain" [8]. European Malignant Hyperthermia Group (EMHG) guidelines recommend prompt actions as soon as the diagnosis is made [9]. These include:

- immediate discontinuation of all potentially triggering drugs,
- call for help,
- increase minute ventilation 2–3 times normal, with 100% oxygen,
- stop the surgery or convert to non-trigger anaesthesia,
- remove the vaporizer, do not waste time on changing the breathing circuit,
- administer dantrolene.

The only pharmacological agent offering causal treatment of HM crisis is dantrolene. Dantrolene depresses excitation-contraction coupling in skeletal muscle by binding to ryanodine receptor 1, and decreasing intracellular calcium concentration [10]. The initial dose of dantrolene is 2–2.5 mg kg^{-1}, the dose should be repeated every 5 min until the patient's stabilization, and the maximum dose is 10 mg kg^{-1} per day, but higher doses are permissible, if necessary.

Symptomatic treatment: cooling (cold fluids IV or gastric and bladder lavage, cold compresses), correction of electrolyte disorders, promotion of diuresis (fluids) must be provided as well. The HM crisis is potentially fatal – before introducing dantrolene the mortality rate was as high as 80% [11].

According to EMHG guidelines a patient with a family history of MH or unexplained intraoperative deaths, unclear anaesthesia complications, postoperative or exertional rhabdomyolysis, or exertional heat stroke requiring hospitalization should undergo the diagnostics for MH susceptibility. The diagnostic pathway is widely described by EMHG [9].

Our case is the best evidence that the knowledge about MH should be constantly refreshed.

A single dose of dantrolene administered at the very beginning of the episode stopped the hypermetabolic cascade. Prompt diagnosis saved the boy's life and prevented serious complications. Our patient had neither a history of complicated anaesthesia nor any neuromuscular problems. Moreover, his family history was unremarkable. Nevertheless, an MH episode developed. Anaesthesiologists must be aware that although very rare, MH exists and can occur unpredictably. Dantrolene should be available wherever anaesthesia is performed.

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