

CASE REPORT

Malignant hyperthermia, a rare perioperative complication: case series and literature review

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Abstract

Malignant hyperthermia is a rare complication of general anesthesia appearing as an acute and potentially lethal hypermetabolic state in people carrying a genetic anomaly expressed in skeletal muscles. Malignant hyperthermia has been scarcely described in sub-Saharan Africa. Herein, we present three cases of malignant hyperthermia occurring in the perioperative period in Cameroon. The authors wish to draw attention to the clinical presentation of this rare but potentially lethal emergency, for timely diagnosis, management and follow-up geared at preventing perioperative mortality.

INTRODUCTION

Malignant hyperthermia (MH) is an autosomal dominant disorder which manifests as a life-threatening hypermetabolic crisis of skeletal muscles [1]. Its incidence is 1 per 5000 to 100 000 patients [2, 3]. There are little or no reports on MH in sub-Saharan Africa. Herein, we present three cases of MH occurring in the perioperative period in two tertiary Cameroonian hospitals which occurred between 2018 and 2019.

CASE REPORT

Case 1

A 22 kg 6-year-old, American Society of Anesthesiologists (ASA) 2 girl with suspicion of Down syndrome was operated for strabismus under general anesthesia (GA). She was hospitalized thrice for both acute otitis media and pneumonia since birth.

Her past surgical, social and family history was uneventful. GA was induced with fentanyl 44 µg, propofol 66 mg and suxamethonium 22 mg followed by orotracheal intubation. GA was maintained using halothane at 1–2%. About 90 min postoperatively, her pulse and temperature suddenly rose from 126 to 166 beats per minute and 37 to 42°C associated with generalized muscular rigidity, and consecutively an episode of generalized tonic convulsions, bradycardia then cardiac arrest. Management involved cardiopulmonary resuscitation and cooling. Dantrolene was not available in the hospital. The patient had a fatal outcome within 30 min of cardiac arrest.

Case 2

A 20 kg 6-year-old, ASA 2 boy with cerebral palsy was operated for bilateral cryptorchidism under GA induced using fentanyl 40 µg, propofol 60 mg and suxamethonium 20 mg followed by

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Table 1: Criteria used in the clinical grading scale for malignant hyperthermia [7]

| Clinical finding | Manifestation |
|----------------------|--|
| Respiratory acidosis | End-tidal CO ₂ > 55 mmHg; PaCO ₂ > 60 mm Hg |
| Cardiac involvement | Unexplained sinus tachycardia, ventricular tachycardia or ventricular fibrillation |
| Metabolic acidosis | Base deficit > 8 mEq/l and pH < 7.25 |
| Muscle rigidity | Generalized rigidity; severe masseter muscle rigidity |
| Muscle breakdown | Serum creatinine kinase concentration > 20 000/L units; cola colored urine; excess myoglobin in urine or serum; plasma [K ⁺] > 6 mEq/l |
| Temperature increase | Rapidly increasing temperature; T > 38.8°C |
| Family history | Consistent with autosomal dominant inheritance |
| Other | Rapid reversal of MH signs with dantrolene. Elevated resting serum creatinine kinase concentration. |

PaCO₂: Arterial partial pressure of carbon dioxide

orotracheal intubation. His past history was uneventful. GA was maintained with isoflurane at 1–2%. About 15 min after induction of GA he developed tachycardia at 172 beats per minute, masseter muscle rigidity which rapidly progressed to generalized muscular rigidity and his temperature rose from 37 to 40°C. Isoflurane was stopped, the anesthesia circuit was changed and orchidopexy was quickly terminated. Dantrolene was administered thrice and cooling was done. His temperature dropped to 36.8°C, pulse 88 beats per minute and signs of muscle rigidity disappeared. Postoperatively, the child did not regain spontaneous ventilation and consciousness. He was transferred to the intensive care unit (ICU). He died on Day 5 post-operation while still unconscious and ventilated.

Case 3

A 44 kg 13-year-old, ASA 1, boy operated for appendectomy via laparoscopy under GA. His past history was uneventful. The induction was done using fentanyl 88 µg, propofol 132 mg and suxamethonium 44 mg relayed with rocuronium 26 mg. He was intubated and GA was maintained with isoflurane at 1–2%. A suppurated retro-caecal appendix was visualized on laparoscopy and was difficult to resect, hence, finally resected via open surgery. At about 105 min of surgery, his temperature suddenly rose from 37 to 39°C, associated with tachycardia at 158 beats per minute and generalized muscular rigidity. Isoflurane was stopped, the whole anesthesia circuit was changed, and surgery was quickly terminated. Dantrolene was administered twice and cooling was performed. Thereafter, his temperature dropped to 36.8°C and all other signs disappeared within 30 min of resuscitation. Postoperatively, the child did not regain spontaneous ventilation and full consciousness. He was transferred to the ICU. On Day 1 post-operation he regained full consciousness and was weaned from mechanical ventilation. On Day 2 post-operation he developed an acute kidney injury complicated by uremic encephalopathy and metabolic

acidosis refractory to medical treatment, hence, requiring three sessions of hemodialysis by Day 5 post-operation. Thereafter, his level of consciousness, serum urea, serum creatinine and serum bicarbonate levels returned to normal. He was discharged home on Day 15 post-operation and referred to a Nephrologist for follow-up.

DISCUSSION

MH is a pharmacogenetic disorder of skeletal muscles that presents as an acute hypermetabolic state when exposed only to the following anesthetic agents: volatile halogen hypnotic gases such as halothane, isoflurane, sevoflurane, desflurane and the depolarizing muscle relaxant such as suxamethonium [2, 4, 5]. The genetic anomaly is located on the Ryaodine receptor gene (RYR1) on chromosome 19 of skeletal muscles [1].

Risk factors for MH include a family history of MH, inherited myopathy, GA using the aforementioned triggering drugs, young age and male gender [1, 4, 6]. The peak age of incidence is between 4 and 14 years [1, 4], as observed in our series of three children aged between 6 and 13 years. The diagnosis of MH is mainly based on clinical grounds [4]. The principal diagnostic features are unexplained elevation of end-tidal carbon dioxide concentration (ETCO₂), muscle rigidity, tachycardia and hyperthermia [4]. MH may occur at any time during GA as well as in the immediate postoperative period as seen in Case 1 presented above. The first warning signs are tachycardia, a rise in ETCO₂ and muscle rigidity [4]. Body temperature elevation is a sign of severity often occurring late and is an important confirmatory sign [4]. A clinical score was designed by Larach et al. [7] to assist in clinical diagnosis (Table 1). Patients with a minimum of six criteria out of eight are rated to have MH using this score. We could not apply this score to all patients due to the absence of a blood gas analyzer, a capnometer and no serum creatinine kinase and kalemia measured. Nonetheless, Cases 1, 2 and 3 had at least three criteria of this score (Table 1).

Uncontrolled hypermetabolic crises lead to anaerobic metabolism that manifests as metabolic acidosis [4]. If unaddressed, rhabdomyolysis, severe hyperkalemia and myoglobinuria occur leading to acute kidney injury (AKI) as seen in Case 3 above [4]. While further consideration and evaluation for differential diagnoses (sepsis, thyrotoxicosis, pheochromocytoma) may continue if the clinician has significant suspicion for MH, empiric treatment with dantrolene and other measures should occur immediately. Important ancillary treatments include stopping all triggering anesthetic drugs; cooling and treating hyperkalemia [1, 6]. Meanwhile, where possible, the affected patient and his family relatives should be screened through *in vitro* contracture tests and DNA testing in search of RYR1 mutations [4]. These were the limitations of this study.

To end, this case series highlights the clinical diagnosis and triggering anesthetic drugs of MH for clinicians working in low-resource settings. This will help in early diagnosis and management of this rare and potentially lethal perioperative emergency.

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CONFLICT OF INTEREST

No conflicts of interest.

ETHICAL APPROVAL

No ethical approval is required for case reports and case series studies according to the Ethical Committees' guidelines of the Yaoundé Central Hospital and the Yaoundé Gynaeco-Obstetric and Pediatric Hospital.

CONSENT

A signed written informed consent was obtained from the parents of all three children presented in this study.

GUARANTOR

Jacqueline Ze Minkande.

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