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CASE REPORT **ANESTHESIA & CONCURRENT DISEASE**

A rare case of late onset malignant hyperthermia

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Abstract

A 42-year-old man with neck squamous cell carcinoma underwent awake fiberoptic intubation and tumor resection under general anesthesia. He developed malignant hyperthermia several hours into the surgical procedure. This case highlights malignant hyperthermia's (MH) variable time course, pathognomonic signs, and the need for rapid diagnosis and treatment. Early recognition and treatment led to rapid resolution of MH. Ongoing discussion of MH is imperative because this disease is often difficult to diagnose early in its time course and may be fatal if not treated expeditiously.

Abbreviations: DS - Dantrolene sodium; DSIS - dantrolene sodium injectable suspension; GA - general anesthesia; MH - malignant hyperthermia; $EtCO_2$ - end tidal carbon dioxide; RYR1 - Ryanodine Receptor gene

Key words: Anesthesia, General / methods; Dantrolene / therapeutic use; Diagnosis, Differential; Humans; Malignant Hyperthermia / diagnosis; Malignant Hyperthermia / etiology; Malignant Hyperthermia / physiopathology; Malignant Hyperthermia / therapy

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1. Introduction

Malignant hyperthermia (MH) is a life-threatening reaction to anesthesia that occurs in patients with genetic disorders of skeletal muscle contraction. The disease usually goes undiagnosed until patients are exposed to a volatile anesthetic, succinylcholine, or other triggering agents.[1,2]

MH onset often occurs shortly following induction of general anesthesia (GA), but the time course may be influenced by different anesthetic agents, and may be delayed.[1,2] Dantrolene sodium (DS) is the only pharmacological treatment for MH and dantrolene sodium injectable suspension (DSIS) now reduces preparation time and increase effective blood concentration. In this case, we describe a patient who presented with MH several hours after induction.

2. Case Report

A 42-year-old man (BMI 21.53 kg/m^2, height 5'6", weight 60.50 kg) was scheduled for radical dissection of a left sided neck tumor. The preoperative examination was unremarkable except for the patient's inability to

open his mouth with an inter-incisor distance of less than 3 cm.

The patient was sedated with dexmedetomidine 0.7 mg/kg/h. The nares, oropharynx and trachea were anesthetized with lidocaine 4% spray x 20 cc in divided doses. The patient underwent awake nasotracheal intubation, and tube placement was confirmed with a fiberoptic bronchoscopy. The patient was induced with propofol 100 mg IV and neuromuscular blockade was initiated with rocuronium 50 mg IV. GA was maintained with sevoflurane.

The surgery proceeded without complications until 272 min after induction, when the end tidal carbon dioxide ($EtCO_2$) began to rise (Figure 1). Minute ventilation was increased, but the $EtCO_2$ continued to increase rapidly. The attending anesthesiologist was called into the room. Sevoflurane was discontinued, the CO_2 absorber was replaced, and the patient was placed on 1.0 FiO2. The possibility of MH was entertained, the surgeons were notified, and a request was made for the MH cart. The patient was started on inj. propofol 150 µg/kg/min IV and inj. remifentanil 0.5 µg/kg/min IV.

The patient's temperature began to rise. The temperature of the room was lowered, the fluid warmers were turned off, and the Bair Hugger was switched to ambient mode. Despite these measures, the $EtCO_2$ rose to 135 mmHg over the ensuing 10 min and the body temperature increased to 39.7°C. The patient developed tachycardia to 135 bpm and hypotension to 60/40 mmHg.

When the MH cart arrived, carbon filters were inserted into the breathing circuit to remove residual sevoflurane and the DSIS was mixed according to instructions. The first DSIS dose 2.5 mg/kg IV was given and was followed by a repeat dose of 2.5 mg/kg IV approximately 4 min later. The Malignant Hyperthermia Association of the United States (MHAUS) hotline was called to confirm treatment.

Following DSIS administration, hypercarbia resolved within 15 min and acidosis resolved within 30 min. The temperature normalized over the next hour. Urine output was measured every 20 min and mannitol was ready to use in the event of rhabdomyolysis, but urine color remained clear. Hyperkalemia was managed by glucose and insulin administration, and DSIS 2.5 mg/kg IV bolus given every 4 h until the end of the surgical procedure.

The patient remained intubated and was transported to the ICU with propofol and fentanyl infusions. The DSIS

Figure 1. Physiologic parameters and anesthetic events during malignant hyperthermia

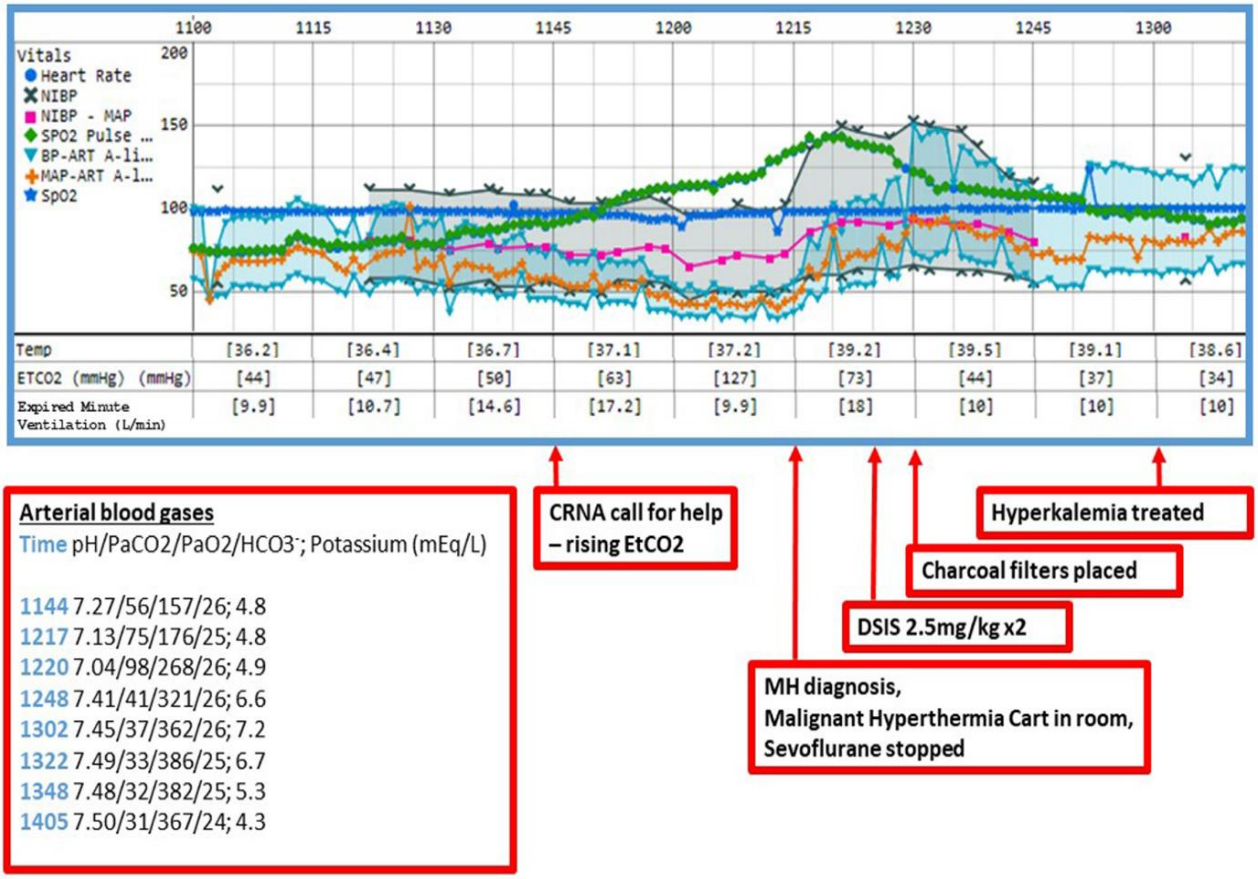
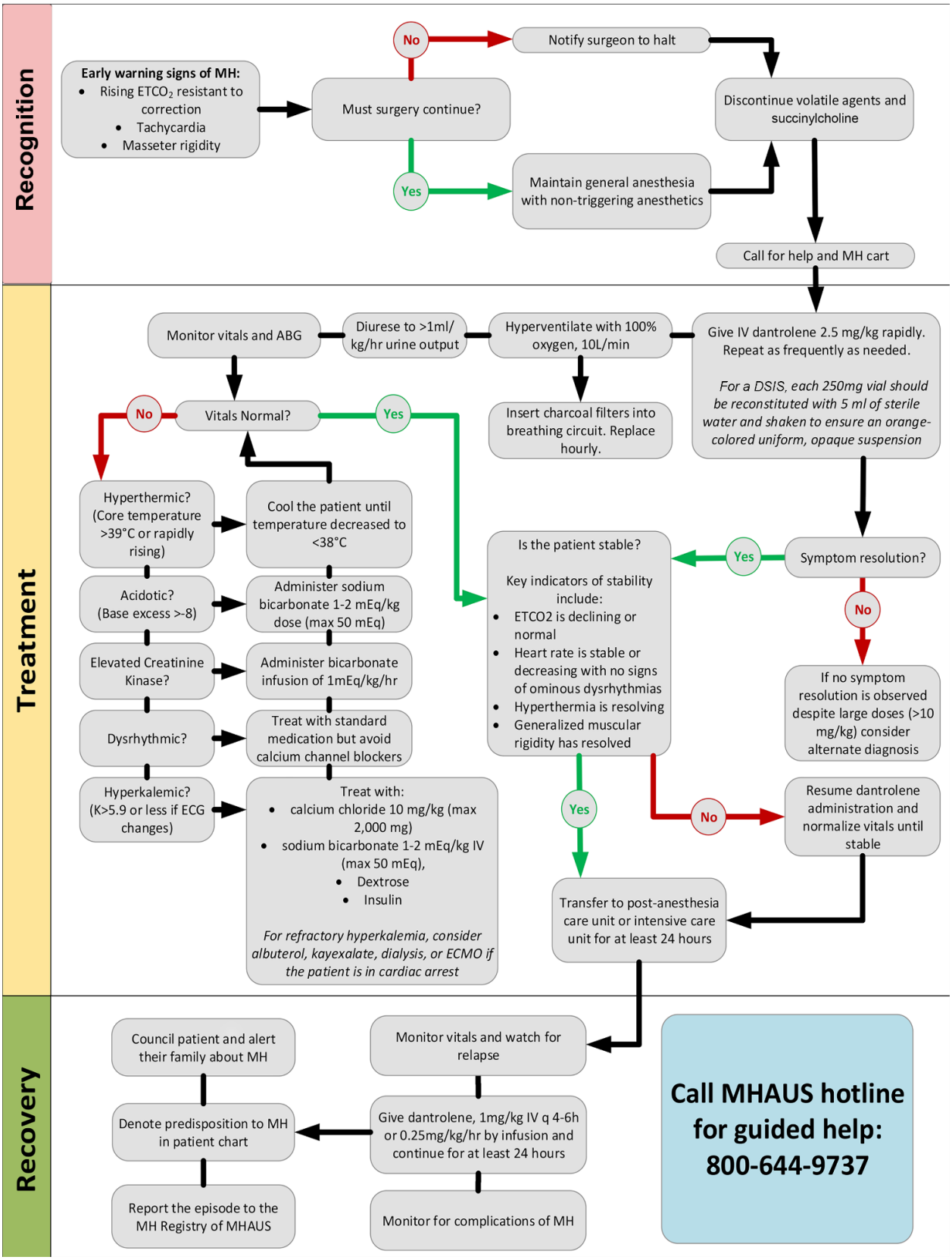


Figure 2. Treatment Algorithm for Malignant Hyperthermia



dose was reduced to 1 mg/kg every 4 h, for a total of 24 h in the ICU. Vital signs remained stable, and the patient was extubated the following day.

The patient's chart was updated to reflect his reaction to MH triggering agents, and the patient was counselled.

3. Discussion

MH is characterized by an uncontrolled release of calcium from the sarcoplasmic reticulum that induces excess skeletal muscle contraction. A mutation in ryanodine receptor gene (RYR1) is most commonly implicated, but the condition exhibits locus heterogeneity.[4] In MH, heat, lactate, and electrolyte imbalances from unabated muscular contractions causes acidosis, hypercapnia, tachycardia, hyperthermia, muscle rigidity, and rhabdomyolysis.[5] DS, the only pharmacological treatment for MH, antagonizes RyR1 receptors to inhibit sarcomeric calcium release.[6] Rapid administration of DS is associated with positive outcomes following an MH episode.[5]

Unfamiliarity with this rare condition can delay treatment. Early physiologic changes can be mistaken for other pathologies like sepsis or serotonin syndrome.[3] Warning signs of MH include surging $EtCO_2$ values and tachycardia that is resistant to corrective efforts without a discernible cause. Masseter muscle rigidity, acidosis, and rising body temperature are also common.[2,4] In this case, the indolent rise in $EtCO_2$ after induction that transformed into precipitously increasing $EtCO_2$ levels triggered the call for help and allowed for prompt diagnosis. Hyperthermia, tachycardia, and hypotension followed shortly thereafter. DSIS doses resulted in rapid clinical recovery and allowed for surgical completion. The protocol for treating MH has been summarized in Figure 2.

DS has few side effects when administered acutely and should be administered whenever MH is suspected.[6] One may administer DS 2.5 mg/kg and up to 10 mg/kg as needed[6]. DS therapy should continue in the ICU at 1 mg/kg IV Q4-6 hours for 24 to 48 hours, with intervals extended to Q8-12 hours once the patient has been stable for more than 24 hours.[8,9]

DSIS has several advantages over generic DS: a smaller volume (one 250 mg vial/5 ml sterile water versus nine 20 mg vials/60 mL sterile water for a 70 kg patient)[10], shorter preparation time (less than1 min versus more than 22 min),[10] lower mannitol concentration (125 mg/vial versus 3 g/vial),[8] faster effective blood concentration (50 mg/ml versus 0.33 mg/ml),[8] and more convenient storage (3 vials on-site versus 36).[7,9] DSIS, however, has a shorter shelf life (33 months versus 36 months)[8] and increased cost per milligram ($13.54/mg versus $4.25/mg).[11]

Most MH cases occur without prior history. This case is an example of late manifesting MH in which prompt diagnosis and treatment was lifesaving. Although rarely, very heroic measures taken without wasting a second may save a life without the availability of the DS or DSIS,[12] it is prudent that at least any one of the two is made readily available, in all healthcare institutions, where surgery is being done.[13]

4. Conflict of interest

Authors declare no conflict of interest. No external or industry funding was involved.

5. Authors' contribution

RV: Chart review, manuscript writing and editing, figure creation and editing, submission oversight

RK: Concept, case information, chart review, manuscript writing and editing

RC, KK: Manuscript editing, figure creation and editing

CN: MH background, figure editing

GR: Case information, manuscript writing and editing, submission oversight

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