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IS IT EXERTIONAL HEATSTROKE OR SOMETHING MORE? A CASE REPORT

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□ **Abstract—Background: Heat stroke, heat-related illness, and malignant hyperthermia all present with hyperthermia. The former two are common presentations in the emergency department (ED). On the other hand, malignant hyperthermia (MH) is an uncommon but equally dangerous condition that requires prompt recognition and specific treatment with dantrolene sodium and avoidance of certain medications to reduce morbidity and mortality. Recent research focusing on nonanesthetic or exercise-induced MH has demonstrated a relationship between certain gene mutations and malignant hyperthermia susceptibility. Case Report: We report the case of a 19 year-old man with a family history of MH who was treated for exertional heat stroke, but despite cooling and adequate fluid resuscitation, demonstrated worsening rhabdomyolysis that subsequently responded to the administration of dantrolene sodium. Why Should An Emergency Physician Be Aware of This?: This case illustrates the importance of recognizing the potential relationship between exertional heat stroke and malignant hyperthermia. The overlap between heat stroke and malignant hyperthermia susceptibility has important implications in the treatment and evaluation of patients presenting with signs and symptoms of heat stroke or heat-related illness in the ED.** © **2016 Elsevier Inc. All rights reserved.**

□ **Keywords—heat stroke; heat-related illness; malignant hyperthermia; exertional heat illness; exertional rhabdomyolysis; dantrolene sodium**

INTRODUCTION

Heat stroke and heat-related illness are common presentations in the emergency department (ED), whereas malignant hyperthermia (MH) is an uncommon but equally dangerous condition that requires prompt recognition and specific treatment to reduce morbidity and mortality. Hyperthermia is a hallmark of all three, making differentiation difficult. The prevalence of malignant hyperthermia susceptibility is estimated at about 1:10,000 to 1:220,000, with the incidence of susceptibility genes estimated at 1:2000 to 1:3000 (1,2). Recent research focusing on nonanesthetic or exercise-induced MH has demonstrated a relationship between certain gene mutations and malignant hyperthermia susceptibility. There are thought to be at least 30 different mutations of the gene associated with the ryanodine (RyR1) or dihydropyridine (DHP) receptors (3,4). Consequently, it is believed that carriers of the malignant hyperthermia susceptibility (MHS) genes may be at increased risk of exertional heat illness (EHI) and exertional rhabdomyolysis (ER), and in some cases even during trivial or previously tolerated levels of exertion (4,5). The overlap between heat stroke and malignant hyperthermia susceptibility has important implications for the evaluation and treatment of patients presenting with signs and symptoms of heat stroke or heat-related illness in the ED.

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CASE REPORT

A 19-year-old man with no known past medical history presented to the ED by air ambulance with altered mental status and hyperthermia. The patient had been playing soccer outside and collapsed during a cool-down run. The ambient temperature at the time was 24.4°C (76°F), 50% humidity, negligible heat index, and fair skies. On scene the paramedics noted he was diaphoretic, confused, and aggressive. The patient was initially hypoglycemic, with a fingerstick glucose of 50 mg/dL, which improved to 230 mg/dL with administration of 25 grams of dextrose (50 mL D50W). He was sedated with 160 mg ketamine intravenous (i.v.), paralyzed with 160 mg of succinylcholine i.v., and intubated for continued agitation and transport to the ED via air ambulance. Of note, the patient's esophageal temperature was reported to be 37.5°C (99.5°F). However, prehospital personnel felt this reading was inaccurately low given the patient's initial tactile temperature. Furthermore, despite external cooling during transport, the patient was hyperthermic on arrival to the ED.

In the ED, initial vital signs showed a heart rate of 133 beats/min, blood pressure of 132/60 mm Hg, and a rectal temperature of 39.5°C (103.1°F). His skin was hot without diaphoresis, and the physical examination revealed no other abnormalities. In the setting of exercise, he was thought to be suffering from exertional heat stroke. Ice packs were placed in the axilla and groin and an external cooling system initiated. The patient was sedated with propofol and was paralyzed with 10 mg of vecuronium i.v. for shivering. His temperature improved over the course of an hour to 38.1°C (100.6°F). During the patient's ED course, his father reported a personal history of malignant hyperthermia, raising concern for exercise-induced MH.

The patient's blood tests were significant for venous blood gas pH of 7.21, a partial pressure of carbon dioxide of 56 mm Hg, despite appropriate ventilator settings. His venous lactate was 5.4 mmol/L. White blood cell count was 11.5, potassium 4.4 mmol/L, creatinine (Cr) 2.39 mg/dL, and anion gap 18. Creatinine kinase (CK) was 1328 U/L, and glucose was 104 mg/dL. Urine toxicology was negative except for benzodiazepines, which he received in the ED.

His chest X-ray study (CXR) was normal, with no focal consolidations or infiltrates. Noncontrast computed tomography of the brain was normal.

The patient was admitted to the intensive care unit (ICU) for further management and evaluation. He was noted to have rhabdomyolysis with peak CK of > 40,000 U/L, acute kidney injury with Cr of 2.39 mg/dL, elevated cardiac enzymes with a Troponin I that peaked at 3.052 ng/mL (reference < 0.014), and elevated transaminases. His disseminated intravascular hemolysis (DIC) panel was negative. He was aggressively fluid resuscitated, and bicarbonate treatment was initiated in the setting of rhabdomyolysis. The patient was intermittently febrile to max 38.1°C (100.6°F), but subsequently improved over the first 24 hours. Urine cultures and blood cultures and repeat CXRs were negative for infection. He was extubated on hospital day 2. The patient had a normal electrocardiogram, a normal cardiac echogram, and his cardiac enzymes trended down. He was then transferred from the ICU to the general medicine floor on hospital day 3. The patient's CK remained elevated on hospital day 4 despite resolution of his fever and other laboratory abnormalities. In the setting of a family history of malignant hyperthermia, physicians from the Malignant Hyperthermia Association and anesthesia were consulted for persistent rhabdomyolysis. Expert consultants recommended the patient be transferred back to the ICU for a dantrolene infusion. He was given 1 mg/kg dantrolene every 6 hours for 24 hours, at which point his CK began to decline (Figure 1). The patient continued to improve and was discharged with no neurological or physical sequelae of his disease.

An extensive MH work-up was initiated. The patient's father consented to genetic testing in the setting of his prior positive calcium uptake testing in the 1980s, however, his more recent specific RyR1 genetic testing was negative, and he did not undergo further muscle contracture testing. Given the extensive number of genes thought to be responsible for MH, the father may have another genetic mutation that makes him susceptible. Our patient later underwent muscle biopsy testing, which showed normal skeletal muscle pathology but revealed a positive caffeine halothane contracture test. Contracture testing is considered the gold standard when testing for MHS. In light of these results, our patient is now considered susceptible to MH.

DISCUSSION

Hyperthermia is characterized by an elevated and uncompensated core body temperature in the setting of normal hypothalamic temperature set point. Clinical history and response to antipyretics can be helpful in distinguishing hyperthermia from fever. It is important to recognize hyperthermia, as it may be rapidly fatal and its treatment differs from that of fever. The most common cause of hyperthermia is exertional heat stroke, typically after intense exercise in a hot and humid environment (4,6). Heat stroke may also be seen with the use of certain medications that interfere with