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Case Report

Experience of Malignant Hyperthermia in a COVID-19 Patient During Urgent Surgery for Necrotizing Fasciitis

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Abstract

Surgical patients with novel coronavirus disease (COVID-19) add complexity in the perioperative period. We experienced a case of suspected malignant hyperthermia (MH) in a COVID-19 patient with a history of intravenous multi-drug abuse undergoing emergent fasciotomy for necrotizing fasciitis. At the end of the procedure, the patient became hypercarbic, hypotensive, and hyperthermic. Intraoperative differential included rhabdomyolysis, septic shock (secondary to necrotizing fasciitis or possibly COVID-19) versus MH. Dantrolene was given with resolution of hyperthermia and hypercarbia. This may be the first case of MH in the setting of severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) infection.

Keywords: *Malignant Hyperthermia; COVID-19*

Abbreviations

ABG: Arterial Blood Gas; Bpm: Beats Per Minute; COVID-19: Novel Coronavirus Disease; ED: Emergency Department; EQUATOR: Enhancing the Quality and Transparency of Health Research; $ETCO_2$: End Tidal Carbon Dioxide; HEPA: High-Efficiency Particulate Air; LRINEC: Laboratory Risk Indicator for Necrotizing Fasciitis; MAP: Mean Arterial Pressure; MH: Malignant Hyperthermia; OR: Operating Room; RYR1: Type 1 Ryanodine Receptor; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2

Introduction

Malignant Hyperthermia (MH) is a pharmacogenetic disorder in which genetic mutations combined with exposure to a triggering agent produces uncontrolled skeletal muscle hypermetabolism. MH is most commonly caused by a mutation to the type 1 ryanodine receptor (RYR1) in skeletal muscle [1]. Exposure to triggering agents in patients with an abnormal RYR1 gene can lead to uncontrolled accumulation of calcium in the intracellular space of skeletal myocytes, leading to hyperthermia, hypercarbia, hyperkalemia, tachycardia, hemodynamic instability, acidosis, and/or generalized rigidity [2]. This is a rare disorder, with an estimated prevalence in New York State of 1:100,000 surgical patients [3]. Diagnosis can be challenging when patients present with acute manifestations of other comorbidities that share nonspecific signs of MH. The following case report shows this challenge during the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic at our institution in New York City.

This manuscript adheres to the applicable Enhancing the Quality and Transparency of Health Research (EQUATOR) guideline, and informed consent was obtained from the patient, as well as written authorization to disclose protected health information was obtained from the patient.

Case Presentation

We present a case of a 36-year-old male who presented to our emergency department (ED) with five days of increasing swelling of left upper extremity following intravenous heroin injection. The patient had circumferential erythema and severe swelling on exam. Patient had a Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score of 8, highly suggestive of necrotizing soft tissue infection [4]. The patient was started on vancomycin and piperacillin-tazobactam and brought to operating room (OR) for debridement. On preanesthetic interview the patient denied any prior anesthetic exposure. He endorsed intravenous heroin and cocaine abuse, last used one day prior

to surgery. He denied any major past medical history. Height and weight were measured at 170 cm and 53.5 kg respectively. Given the novel coronavirus disease (COVID-19) pandemic affecting the area, the patient was tested for SARS-CoV-2 preoperatively via RT-PCR from nasopharyngeal swab and found to be positive. He was transported to a negative pressure room in the preoperative area following the results of his SARS-CoV-2 test. The patient endorsed chest tightness that he attributed to the expanding edema in his upper extremity, but otherwise denied respiratory symptoms during preoperative interview. He reported tactile fever prior to presentation, but was afebrile in the preoperative area prior to surgery. Given his COVID-19 positive status, negative pressure OR was assigned to the case, and the OR was cleared of nonessential equipment to prevent viral contamination. High-efficiency particulate air (HEPA) filter was placed at the expiratory limb of the anesthesia circuit. All anesthesia providers wore N95 masks and protective equipment consistent with American Society of Anesthesiologists and Anesthesia Patient Safety Foundation recommendations for COVID-19 positive patients [5].

A 20 gauge IV was placed in the right antecubital vein. General anesthesia was induced with propofol 3.7 mg/kg and neuromuscular blockade achieved with rocuronium 1 mg/kg. A higher than typical dose of propofol was used to ensure adequate induction given the patient's substance abuse history. Rapid sequence induction with video laryngoscopy was performed consistent with hospital policy for all COVID-19 patients. Intubation was performed without complication. Anesthesia was maintained with sevoflurane 1.3% - 2.4% and surgery was initiated. The surgery team began debridement and immediately encountered purulent material. During debridement the patient became increasingly tachycardic from 108 beats per minute (bpm) preoperatively to > 130 bpm. Tachycardia persisted despite 2 liters of intravenous fluid and 2 mg of hydromorphone.

One hour following initial incision, the surgery team began irrigation in preparation for packing and dressing the wound. The patient was transitioned to pressure support ventilation with 100% FiO_2 in preparation for extubation. The patient was noted to be initiating breaths over 30 times per minute with tidal volumes > 8 cc/kg with end-tidal sevoflurane of 1.5%. End-tidal carbon dioxide ($ETCO_2$) was < 40 mmHg. As the surgery team packed and dressed the wound, the patient became increasingly and rapidly hypotensive. A phenylephrine drip was started and rapidly up-titrated to 200 mcg/min to maintain mean arterial pressure (MAP) > 65mmHg (See figure 1). $ETCO_2$ had risen above 50 mmHg. An additional 18 gauge IV was placed on his right upper extremity. An arterial line was placed; point-of-care arterial blood gas (ABG) showed a pH of 7.24, $PaCO_2$ of 65 mmHg, bicarbonate 28.3mmol/L, lactate of 5.5 mmol/L, and potassium of 6.1 mmol/L. At that time base excess was -0.3 and glucose was 162 mg/dL. Intraoperative EKG monitor was noted to have sinus tachycardia with peaked T waves. The patient was warm on skin exam and nasopharyngeal temperature was > 40°C. Additional anesthesia providers and technicians were called for assistance. 5 U Insulin, 12.5g of 50% dextrose, and 1g calcium chloride were given for hyperkalemia. They helped bring emergency equipment and drugs into the OR, including a central line kit to facilitate transition from phenylephrine to norepinephrine and vasopressin for management of the patient's hypotension, as we typically administer these agents centrally. Our differential diagnosis included MH, septic shock (from seeding of infection during debridement or possibly COVID-19, however unlikely it may be to cause acute decompensation), rhabdomyolysis, drug withdrawal, cardiogenic shock secondary to cocaine use, and serotonin syndrome (given the patient's polysubstance abuse history). Sevoflurane was stopped and fresh gas flows were increased. $ETCO_2$ continued to uptrend, peaking at 72 mmHg. Propofol infusion was started for sedation at 100mcg/kg/min. An EEG was not placed given the emergent clinical situation and immediate availability, since most of the equipment in the negative pressure OR were removed to prevent viral contamination. The MH kit was brought to the OR and the Malignant Hyperthermia Association of the United States hotline was contacted by the anesthesia team. The patient was transitioned to volume control ventilation, initially with RR 30 and TV 500ml with 100% FiO_2. Rocuronium was re-administered, although the patient was not noted to have masseter, neck or upper extremity rigidity at time of re-administration. The anesthesia circuit and HEPA filter were not changed due to concern for aerosolization of SARS-CoV-2 virus. Instead, charcoal filters were placed between the circuit and anesthesia machine. The patient was cooled with ice packs, and peripheral IV fluid was changed to cold saline to facilitate cooling the patient. A 9 Fr double lumen central line was placed emergently. 2.5 mg/kg dantrolene was given centrally, with rapid reduction in $ETCO_2$. Five minutes after dantrolene administration, $ETCO_2$ uptrended and a second dose of 2.5 mg/kg dantrolene was given. $ETCO_2$ normalized again, and at that time the patient had a pH of 7.37, $PaCO_2$ of 48 mmHg, lactate of 4.0

mmol/L, and potassium of 5.2 mmol/L. The patient was transitioned from phenylephrine to norepinephrine 15 mcg/min and vasopressin 6 units/hr to maintain MAP > 65 mmHg. Laboratory studies sent following this event were significant for a creatine phosphokinase of 268 IU/L, within normal range following fluid resuscitation (ref 64 - 499 IU/L). The patient was transitioned to volume control ventilation at rate 16 RR and TV 450 ml with 100% FiO_2 prior to transport to a temporary ICU for SARS-CoV-2 infected patients.

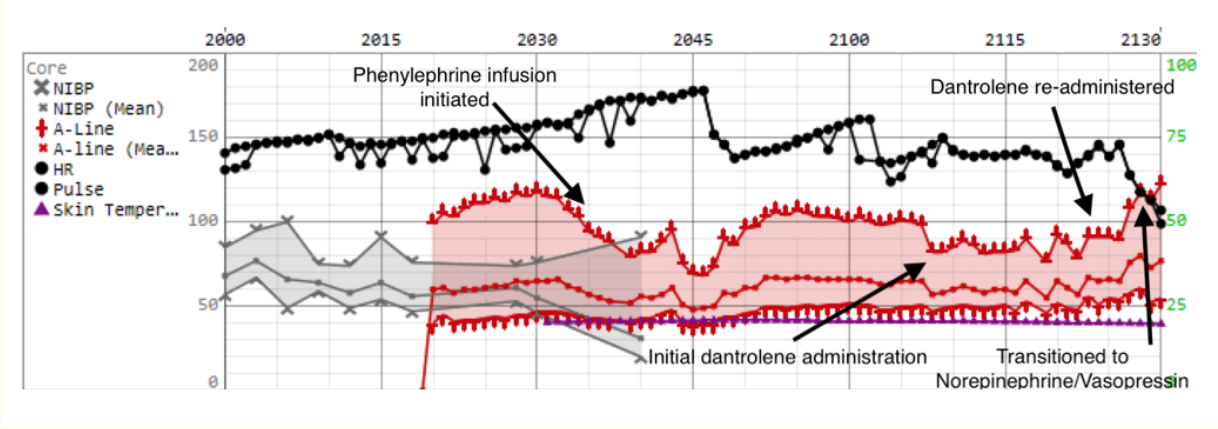

Figure 1: *Hemodynamic monitoring record during this period.*

The patient was transferred to the ICU intubated using a transport ventilator still with a HEPA filter in place on his endotracheal tube, with plans to return to the OR the next day for further debridement. Prior to transfer, core temperature fell below 37°C, requiring removal of ice packs and placement of a forced-air warming blanket. Urine output during the case was 50cc of dark yellow urine, but overnight output increased to 550cc of dark yellow urine. Urine output continued to increase in volume and clarity over the next day. Urine myoglobin was 2 mg/L the morning following the case. Norepinephrine and vasopressin were weaned to 3mcg/min and 2.4 units/hr by the next morning. The patient returned to the OR the next day for re-operative debridement. Departmental MH precautions, including flushing of the anesthesia machine with high flow oxygen for over 30 minutes, placement of charcoal filters between the circuit and anesthesia machine, and removal of all triggering agents and vaporizers for volatile anesthetics from the room were observed. The case proceeded without incident. The patient was extubated 4 days after his initial surgical procedure. He underwent general anesthesia for a third time for skin grafting, again with MH precautions in place, and without complications.

Discussion

This case presented a broad set of possible underlying etiologies which could explain this patient's clinical decompensation. Diagnoses consistent with the patient's history and clinical picture included MH, septic shock with acute inflammation from either the debridement or due to COVID-19, rhabdomyolysis, or a drug interaction or withdrawal. Early in the case rhabdomyolysis or acute septic shock seemed more likely given the frank purulence and tissue invasion encountered by the surgical team. Drug interaction was an important consideration given his recent substance use and the possibility that he had used an illicit or prescription drug he had not disclosed on preoperative interview. Ultimately over the course of the case his symptoms became more consistent with MH, and rapidly resolved with dantrolene. Larach., *et al*. described a scale to assess the likelihood that an adverse reaction was indeed MH [6]. This scale assigns point values for common symptoms and vital sign and laboratory abnormalities associated with MH, including tachycardia, hyperthermia, hyperkalemia, elevated creatine phosphokinase, myoglobinuria, and clinical rigidity. Our patient scored 51 on this scale (range 0 to a highest possible score of 113, with values >50 considered almost certain for diagnosis), indicating this event was almost certainly MH.

While this patient's presentation would potentially make him a candidate for a confirmatory caffeine/halothane contracture test [7] this was deferred given the high clinical suspicion for MH and difficulty coordinating an elective and highly specialized procedure during the pandemic. The patient was treated as MH-susceptible for the remainder of his hospitalization and was educated on discussing this with future anesthesia providers.

The patient's COVID-19 infection presented unique complications in this case. While this patient had few symptoms specific to the disease prior to surgery, there have been case reports of viral illnesses triggering MH-like symptoms in susceptible patients [8,9]. There have been reports of rapid progression of respiratory symptoms associated with COVID-19 [10]. In our experience with COVID-19 patients, rapid progression of disease as well as episodes of decompensation even following periods of acceptable respiratory mechanics on a ventilator can occur. COVID-19 is known to cause dysregulated inflammation and there are examples of rapid progression of inflammatory elements of the disease [11,12]. This further complicated diagnosis during the patient's decompensation.

As SARS-CoV-2 has been shown to remain infectious on some surfaces for up to 72 hours, [13] it is our departmental policy to minimize equipment in ORs with infected patients in order to minimize the transmission risk. This has included removing nonessential equipment and as much disposable equipment and medications as possible from the OR to reduce infection risk to staff and future patients. Similar practices have been described at other institutions [14]. Many supplies that are commonly kept in ORs were stored outside for this case. Of note, we experienced this case in early April 2020, where New York City was severely affected by the COVID-19 pandemic. At our institution at the time of this case, many ORs had been converted to temporary intensive care units, further displacing our usual space for anesthesia supplies. This required a coordinated response between the anesthesia staff in the room and technicians and assisting staff outside to get emergency supplies while minimizing environmental exposure and time lost donning and doffing protective equipment. We would like to reinforce that institutions should tailor policies to allow ready access to emergency supplies in COVID-19 positive ORs in ways that preserve patient and provider safety.

Conclusion

This case is, to our knowledge, the first reported incident of MH in a patient with COVID-19. It raised unique considerations including arranging for emergency supplies when treating a COVID-19 patient intraoperatively. It also provides an example of the complications that COVID-19 could present in diagnosing a MH episode or other intraoperative emergency.

Conflicts of Interest

None.

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All authors were employees of New York Presbyterian - Columbia University Irving Medical Center in the Department of Anesthesiology at the time of this case. This work was performed as part of that employment and otherwise did not receive outside funding.

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