

# A Rare Presentation of Malignant Hyperthermia in a Patient With Poliomyelitis

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## Abstract

Malignant hyperthermia (MH) is a rare hypermetabolic response to halogenated anesthetic gases or succinylcholine. We presented a case of malignant hyperthermia in a 39-year-old male with a past medical history significant for poliomyelitis, who had been exposed to anesthetic agents multiple times in the past. The patient presented with MH crisis about 4 h after surgery, with pre operative exposure to succinylcholine. Seventy percent of MH cases are familial ones and sporadic cases are rare. This case report creates awareness of the diagnosis of MH in patients without family history of the disorder and with delayed symptom onset. Studies are lacking on the pathophysiology of MH in patients with neuromuscular disorders since these patients might have atypical presentation.

**Keywords:** Malignant hyperthermia; Poliomyelitis; Succinylcholine; Dantrolene

## Introduction

Malignant hyperthermia (MH) is defined as a disturbance of the skeletal muscle calcium homeostasis, triggered by volatile anesthetics and depolarizing muscle relaxants (i.e., all halogenated inhalational anesthetics such as halothane, isoflurane, sevoflurane and the depolarizing muscle relaxant succinylcholine). The gene for the ryanodine receptor *RYR1* is the primary site for mutations linked with MH, but other genetic loci have been identified such as *CACNA1S* and *STAC3* [1]. Clinical features of MH include: tachycardia, tachypnea, hypoxemia, hypercarbia, metabolic and respiratory acidosis, hyperkalemia, cardiac dysrhythmias, hypotension, skeletal muscle rigidity, and hyperthermia. The main stay of treatment for MH is im-

mediate dantrolene administration [1] and other supportive measures in correcting hyperthermia, acidosis, hypoxemia, arrhythmias and preserving renal function. Supportive measures include: providing a patent airway by intubation, cooling blanket for hyperthermia, anti-hypertensive medication drips for hypertension, adequate IV fluid hydration etc.

## Case Report

A 39 years old male with a past medical history significant for poliomyelitis of the left lower extremity was admitted for elective perianal fistulotomy for an unhealing perianal fistula. Due to poliomyelitis, the patient had left lower extremity atrophy and weakness. Patient had six minor knee surgeries and appendectomy without any issues. During the procedure, the patient was intubated and received fentanyl, lidocaine, succinylcholine, propofol. Patient had an uncomplicated extubation in the recovery room. Patient was recovering well with normal vital signs until 3 h postoperative. He complained of shaking, chills and gradually his temperature went up to 40.1 °C in the subsequent 2 h. Four hours postoperative, his vitals were: blood pressure (BP) 200/110 mm Hg, pulse 125 bpm, RR 33 breaths/min, T 40 °C. The patient was immediately transferred to ICU. Patients labs revealed potassium: 5.1; anion gap: 15; CK: 2089, arterial pH: 7.15; arterial pCO<sub>2</sub>: 58; arterial pO<sub>2</sub>: 67; arterial pHCO<sub>3</sub>: 19.8; FiO<sub>2</sub>: 55%; SpO<sub>2</sub>: 86%.

Based on the clinical and lab findings a diagnosis of MH was established. Patient was immediately intubated and received IV dantrolene 2.5 mg/kg; cold normal saline infusion, cooling blankets and was started on labetalol drip. Patient was off labetalol drip in 2 h but his temperature fluctuated between 38.3 - 39.2 °C over the next 2 days. Patient's blood cultures showed no growth. TSH and cortisol levels were within normal limits. Over the next 8 days patient's hospital course was complicated by electrolyte imbalances, respiratory acidosis requiring prolonged intubation, DIC, rhabdomyolysis, fluid overload and acute renal failure. After prolonged ventilator and supportive management the patient was completely weaned off all sedatives/hypnotics and passed the spontaneous breathing trial. On the eighth day of the hospital stay the patient got extubated and was discharged on 2 days later. There was a gradual decline in hemoglobin from 13 to 7.9 and platelet count from 253 to 66 over the next 6 days of dantrolene infusion, which is the most common complication of dantrolene.

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The patient's blood dyscrasia slowly improved and reached baseline in 1 month.

## Discussion

The incidence of MH episodes during anesthesia is between 1:10,000 and 1:250,000 [1]. The syndrome is inherited in an autosomal dominant pattern, although wide variability is reported [1]. The incidence of MH is 1 in 30,000 estimated by Robinson et al [2]. An uncontrolled rise of myoplasmic calcium, which activates biochemical processes related to muscle activation is responsible for the pathophysiologic changes in MH. A defective Ca<sup>2+</sup> channel located in the SR membrane is implicated in MH susceptibility. This channel is termed as ryanodine receptor (RyR1). In most cases, the syndrome is caused by a defect in the ryanodine receptor. Over 400 variants have been identified in the *RYR1* gene located on chromosome 19q13.1, and at least 34 are causal for MH [1]. The channel RyR1 is closely associated with many other proteins, such as the dihydropyridine receptor (DHPR) Ca<sup>2+</sup> channel which is situated in the T-tubule region of the sarcolemma that mediates transfer of voltage change to the RyR1 receptor. Other proteins with potential or known roles in RyR1 function include integral SR membrane proteins i.e., SRP-27, junctate, the transient receptor potential cation channel (TRPC) family and triadin [1]. Proteins that modulate the function of RyR1 include the FK508 binding protein FKBP12, the Ca<sup>2+</sup> binding protein calmodulin, the histidine-rich Ca<sup>2+</sup> protein, HRC and the luminal Ca<sup>2+</sup> buffer calsequestrin. HRC is also a luminal protein known to interact with both triadin and SERCA and has been suggested to have a role in mediating cross talk between SR Ca<sup>2+</sup> uptake and release [1].

Few myopathies are associated with increased susceptibility to MH with confirmed *RYR1* variants. These myopathies include: central core disease (CCD), multiminicore myopathy (MmD) and centronuclear myopathy [1]. Recessive variants in *RYR1* have been associated with MmD, some of which result in altered Ca<sup>2+</sup> release from intracellular stores. Similarly there might be few variants of *RYR1* in neuromuscular disorders like poliomyelitis which may enhance susceptibility or may be associated with delayed onset. However studies are lacking.

About 528 cases of MH were analyzed by North American MH registry out of which 64 cases of MH were postoperative and the mean time for symptom onset was 0 - 40 min for those cases [3]. MH may occur at any time during anesthesia as well as in the early postoperative period, but usually not 1 h after discontinuation of volatile agents [3]. However in our case, the patient developed MH after 4 h of succinylcholine administration, a unique presentation for MH.

An increase in the end-tidal carbon dioxide is a sensitive and early sign of MH [4]. Uncontrolled hypermetabolism leads to respiratory and in most cases metabolic acidosis due to rapid consumption of energy stores and ATP. MH if untreated leads to rhabdomyolysis, life-threatening hyperkalemia; myoglobinuria, and acute renal failure. Additional life-threatening complications include DIC, congestive heart failure, bowel ischemia, and compartment syndrome of the limbs secondary to

profound muscle swelling.

The "gold standard" for diagnosis of MH is currently an *in vitro* contracture test (IVCT), which is based on contracture of muscle fibers in the presence of halothane or caffeine. An individual is considered susceptible to MH when both caffeine and halothane test results are positive. DNA analysis, however, offers an alternative to the IVCT, requiring only a blood specimen.

Dantrolene is the only drug known to specifically treat MH. Dantrolene inhibits the DHPR in an RyR1-dependent manner, binding to a specific site on the RyR1 protein and reducing RyR1 channel activity in intact muscle cells [5, 6]. Hyperthermia is treated with cooling blankets and cold normal saline infusion; and arrhythmias are treated with amiodarone. Electrolyte abnormalities need to be addressed, ventilatory support may be needed and other supportive measures also come into play [1].

## Conclusions

In patients with neuromuscular disorders like poliomyelitis, succinylcholine should be avoided and caution should be exercised with administration of inhalational agent to avoid MH. The susceptibility and timeline between exposure to the triggering agent and symptom onset of MH in patients with neuromuscular disorders may be related to *RYR1* variants similar to muscular dystrophies. However studies are lacking. MH should be high on the differential in cases with the appropriate signs and symptoms suggestive of MH, after there is recurrent exposure to anesthetic agents, no matter what the time line is.

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