A Case of Afebrile Malignant Hyperthermia

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Zachary M. Abid, MD.[1], Kyle S. Malek, M.D.[1]
[1]Honor Health Thompson Peak Internal Medicine, 7400 E Thompson Peak Parkway, Scottsdale, AZ 85255

INTRODUCTION

Malignant hyperthermia (MH) is a life-threatening emergency sometimes referred to as malignant hypermetabolic syndrome.[1,2] Typical presentation occurs soon after induction with general anesthetic triggering agents (e.g., volatile agents or succinylcholine). Initial signs include hypercarbia and tachycardia with ***possible*** hyperthermia.[3] This is followed by generalized muscle rigidity, specifically with the masseter muscle. Part of the difficulty in recognizing this potentially lethal condition is the low incidence of the disease combined with wide variation of initial presentation.

- Incidence 1:100,000 of anesthetic events[4]
-Children under 19 years account for 45 to 52 percent of reported events[4]
- 2:1 male to female[4]

- Skeletal muscle receptor mutation with autosomal dominant inheritance pattern

-Typically, sustained muscle spasm and peripheral vasoconstriction lead to a rise in core temperature, in severe cases as quickly as 1 degree every few minutes.

- History of an uneventful prior exposure is common. Approximately one-half of patients who develop acute MH have had one or two uneventful exposures to triggering agents suggesting that there is a sensitization process and patients with more surgeries are at higher risk.

CASE DESCRIPTION

History
- The patient was a 41-year-old male with depression controlled on SSRI who was having dental implants placed and was nasally intubated.

Exposure
- Isoflurane for induction and succinylcholine for paralytic.

Symptoms
- **Masseter and full body rigidity** that did not respond to more anesthetic. The patient did ***NOT*** develop fever. His anesthesiologist made a call to EMS and he was transferred to the ED.

In the ED
- Persistent rigidity and bilateral lower extremity clonus.

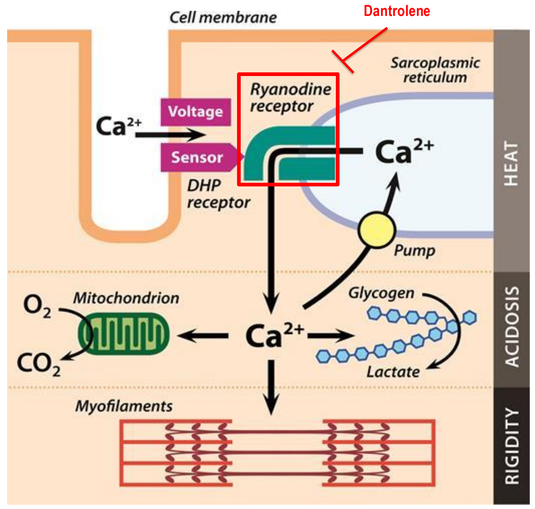
Labs
- (CBC, CMP, CK, and UA) were unremarkable

Vitals
- Temp: 96.6 | HR 104 | RR 18 | BP 118/56 | SpO2 100% NTT

Intervention
- Administration of 2.5 mg/kg Dantrolene
- Admitted to ICU
- Repeat labs were unremarkable.

Although the patient was on an SSRI, the consulting teams felt the patient's clinical presentation was most consistent with MH, likely caused by the anesthetics patient received. He was administered dantrolene and admitted to the intensive care unit for monitoring. The patient had no significant metabolic derangements noted on repeat labs. EEG unremarkable.

Mechanism of Action & Genetics



https://pubs.asahq.org/anesthesiology/article/115/5/915/12913/Malignant-Hyperthermia

Dantrolene works as a direct antagonist to the **Ryanodine Receptor** reducing the efflux of calcium from the sarcoplasmic reticulum, which in turn reduces excitation-contraction coupling.

There is a genetic implication in malignant hyperthermia. A knock-in mouse trial testing the RYR1 gene revealed a direct gene dose-dependent response to anesthetic exposure.[8]

Incidence of Symptoms Assoc. With MH

Clinical Sign	Percentage with signs
Hypercarbia	92.2
Sinus Tachycardia	72.9
Rapidly increasing temperature	64.7
Elevated temperature	52.2
Generalized Muscle Rigidity	40.8
Tachypnea	27.1
Masseter Spasm	26.7
Sweating	17.6
Cola-colored urine	13.7
Cyanosis	9.4
Ventricular Tachycardia	3.5
Excessive bleeding	2.7
Ventricular fibrillation	2.4

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An analysis of reports of MH events to the North American MH Registry from 1987 to 2006 found that elevated or rapidly increasing temperature was one of the first signs noted in only 8.2 percent of cases, and the only initial sign in 3.9 percent, but was among the first three signs of an MH event in over 60 percent of patients with a mean temperature of 39.1°C.
The most reliable symptoms is an increasing ETCO2 despite an adequate or increasing minute ventilation.

DISCUSSION

- This case highlights the difficulty of treating uncommon conditions.
- Part of the difficulty of this case, and others like in the future (secondary to the increased prevalence of SSRI use), is the patient's exposure to Selective Serotonin Reuptake Inhibitors (SSRI's). Primary history, provided by the patient's spouse was not supportive of SSRI overdose. Additionally, the patient's anesthesiologist accompanied the patient to the hospital and recounted that the onset of symptoms occurred soon after anesthetic administration.
- Incidence of MH in the general population is estimated at 1:100,000; however, this is likely an underestimate because of variability in presentation. It should be noted in one review of 255 patients with MH almost 80% had signs indicative of muscular involvement while only 50% had elevated temperature.[5]
- The patient's physical exam had some classic signs of MH in particular severe masseter muscle rigidity. However, the patient seemed to also exhibit other signs that were less consistent with MH and seemingly more consistent with serotonin syndrome (SS) including myoclonus and hyperreflexia.
- Multiple teams were consulted including Toxicology, Neurology, and the ICU.
- There was a concern that if this was a case of serotonin syndrome, that treating with dantrolene would worsen serotonin syndrome however we found no evidence that dantrolene is directly implicated in SS fatality, just not effective.[6,7]
- This patient remained nasally intubated overnight. Repeat labs showed no signs of elevated Creatinine Kinase indicative of rhabdomyolysis and no signs of acute kidney injury.
- The next day, patient responded well to sedation vacation and spontaneous breathing trials. He was extubated, moved out of the ICU to the general floor and made a full recovery.

CONCLUSION

- Malignant hyperthermia is an uncommon life-threating condition with variable presenting symptoms.
- An elevated temperature may only be present in roughly 50% of cases.
- The tell-tale exposure is recent inhaled anesthetics (e.g. isoflurane) and depolarizing neuromuscular blocking (e.g. succinylcholine).
- Treatment is dantrolene 2.5 mg/kg.
- With known history of MH use other anesthetics (etomidate, ketamine, propofol, NO) and Non-depolarizing muscle relaxant (e.g. rocuronium)
- Early recognition is key, and research in the future to identify at risk individuals through possible genetic testing could be helpful.

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