Atypical Presentation of Delayed Onset Malignant Hyperthermia: Internist Needs to Be Aware Of

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Abstract
Malignant hyperthermia (MH) is a rare but potentially life threatening drug related reaction predisposed by genetic factors. Although most cases develop within the intraoperative setting, less commonly, delayed onset presentations have also been reported. With variability in symptoms and time of onset, definitive diagnosis of MH is challenging. Herein, we report a case of a 73-year-old man presented with severe oliguria in the setting of recent surgical procedure. He was found to have acute kidney injury, myoglobinuria, transaminitis and elevated CPK indicative of rhabdomyolysis. He did not present with the typical symptoms of MH and workup revealed no inciting etiologies, i.e. anatomical, infectious, and autoimmune, asides from anesthetic exposure during the intraoperative setting. Recognizing this may prevent the potential of a life-threatening reoccurrence of MH intraoperatively, if appropriately diagnosed.

Keywords
Malignant hyperthermia, Acute kidney injury (AKI), Transaminitis, Rhabdomyolysis

Introduction
Malignant hyperthermia (MH) is a pharmacogenetics syndrome associated with mutations in ryanodine receptor-1 (RYR1) gene responsible for encoding for skeletal muscle ryanodine receptor [1]. The prevalence of MH after administration of anesthesia is estimated to be 1:100,000 [2]. With the possibility of an atypical or mild reaction, this number is likely an underestimate. A majority of cases of MH are triggered after the use of volatile anesthetics (e.g., desflurane, enflurane, isoflurane, sevoflurane, and halothane) and/or succinylcholine [3]. Of the patients who develop acute MH, approximately half had previous exposure to triggering agents with no subsequent reaction [4]. This hypermetabolic response typically presents within one hour of anesthesia in the intraoperative setting with tachycardia, tachypnea, hyperthermia, hyperkalemia, and increase end-tidal carbon dioxide. In rare cases, it may present as severe postoperative rhabdomyolysis with no other symptoms [5,6].

Case Summary
A 73-year-old male with a history of hypertension, benign prostatic hyperplasia, gout, traumatic right BKA presents with complaints of urgency and inability to urinate one day after an outpatient laryngoscopy for evaluation of chronic hoarseness of voice. The patient received succinylcholine, propofol, rocuronium, fentanyl, dilaudid, dexamethasone, glycopyrrolate, neostigmine, and ondansetron intraoperatively. Anesthesia documentation of the procedure noted no contraction of the masseter muscles. The patient had no urinary complaints immediately after procedure. The following morning, the patient noticed that he had urinary urgency with inability to urinate after an outpatient laryngoscopy for evaluation of chronic hoarseness of voice. The patient received succinylcholine, propofol, rocuronium, fentanyl, dilaudid, dexamethasone, glycopyrrolate, neostigmine, and ondansetron intraoperatively. Anesthesia documentation of the procedure noted no contraction of the masseter muscles. 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42 iU/L and 193 iU/L (10-60 iU/L), respectively. The urinalysis showed amber colored urine with large amounts of blood (15-20 red blood cells per high-power field). The differential diagnosis of rhabdomyolysis is very broad, but after extensive workup, to rule out inciting events/etiologies, i.e. anatomical, infectious, autoimmune, the most likely diagnosis for our case was rhabdomyolysis induced by delayed onset MH. He did not present with the typical symptoms of MH of hyperthermia, hypercarbia, tachycardia, or tachypnea [5].

Another possible anesthesia related etiology of the rhabdomyolysis, transaminitis, and myopathy seen in this patient is propofol infusion syndrome. This rare condition characteristically presents with these symptoms after propofol infusions at doses higher than 4 mg/kg/hr for greater than 48 hours [7]. Although the patient presented with these symptoms, the timeline does not correlate properly. The duration of his outpatient surgery was well less than 48 hours, so even if a propofol infusion was used to maintain anesthesia, the duration is shorter than typically associate with this syndrome.

In conclusion, although uncommon, there have been reported cases of patients with this subacute but clinically significant presentation of MH [9]. It is important to have high suspicion of MH for post-anesthesia rhabdomyolysis. Recognizing this may prevent the potential of a life-threatening reoccurrence of MH intraoperatively, if appropriately diagnosed.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Consent for Publication

The patient described in the case report had given informed consent for the case report to be published.

Competing Interest

The authors declare that they have no competing interests.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Author’s Contribution

MAH encouraged MAG and MZS to learn about Malignant hyperthermia and its delayed presentation. All authors discussed the medical literature. MAG presented the idea, MAG, MZS and MAH wrote the manuscript with input from all authors.

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