Difficult Intubation due to an Unexpected Adverse Drug Reaction

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Abstract

Difficult intubation is a challenging problem for the physician. We report a difficult intubation in a patient who had masseter muscle rigidity as an adverse reaction to rocuronium during rapid sequence intubation. The work is also remarkable because, to the best of our knowledge, only seven cases of masseter muscle rigidity (MMR) after administering non-depolarizing muscle agents reported. Moreover, malignant hyperthermia (MH) should be suspected in any patient with MMR. MMR could be independent of MH. The pathophysiology of malignant hyperthermia related to this case is also discussed.

Keywords: Masseter Muscle Rigidity; Neuromuscular Blocking Agents; Malignant Hyperthermia; Intubation

Abbreviations

MH: Malignant Hyperthermia; MMR: Masseter Muscle Rigidity; ROSC: Return of Spontaneous Circulation; CPK: Creatine Phosphokinase; SpO2: Peripheral Capillary Oxygen Saturation; CACNA1S: Calcium Voltage-Gated Channel Subunit Alpha1; RYR1: Ryanodine Receptor 1; CHCT: Caffeine Halothane Contracture Test; LMA: Laryngeal Mask Airway; SSRI: Selective Serotonin Reuptake Inhibitor; ATP: Adenosine Triphosphate; IgE: Immunoglobulin E.

Introduction

Most common airway complications are unanticipated and can lead to harm and death, particularly in the emergency department and the intensive care unit. The most common complications are esophageal intubation (1.3 - 11%), pulmonary aspiration (2.0 - 5.9%), severe hypoxemia of oxygen saturation less than 80% (14.0 - 26.0%), cardiac arrest (1.8 - 3.0%) or difficult airway management of more than 3 attempts to intubate (8.0 - 20%) [1].

Case Presentation

A 50-year-old Hispanic woman had an end-stage renal disease due to diabetic nephropathy and was admitted to the hospital for a cadaveric donor kidney transplant. She had a rejection of the transplanted kidney. After 2 weeks of the transplant, she developed progressive renal failure, dyspnea, and hypoxemia. The patient was diagnosed with volume overload with acute pulmonary edema, which required a transfer to the intensive care unit (ICU).

Because the non-invasive mechanical ventilation with full face mask failed, we proceeded with an orotracheal intubation. The patient had a rapid sequence intubation protocol with etomidate, rocuronium, and a direct curved blade laryngoscopy. As we began the procedure, we noted that the patient had rigidity, disabling her from opening her jaw. The patient was then administered succinylcholine, without any improvement in rigidity.

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The challenge was to open her mouth for intubation. Upon re-inspection, we noted that the rigidity was localized to the jaw. At this point, respiratory ventilation was given via bag-mask ventilation. As oxygenation continued, sinus bradycardia was noticed without pulse indicating pulseless electrical activity. Resuscitation was then initiated with chest compressions, bag-mask ventilation, oxygen, and epinephrine.

The second attempt at intubation was successfully made using video laryngoscope Glidescope® by Verathon (20001 North Creek Pkwy N, Bothell, WA 98011, United States of America). The peripheral capillary oxygen saturation (SpO₂) increased to 85%. While fixing the tracheal tube, the tube was proximally dislodged due to the compression movements during resuscitation. The tube was then pushed forward, and a bronchoscope was used to verify the position. However, we found out that the tube went into the esophagus.

The patient’s nostrils were edematous, unable to advance the tracheal tube through the nose with the bronchoscope. The anesthesiologist was called in. The jaw was more relaxed at this point. A video laryngoscope King Vision® by Ambu (Baltorpbakken 13, DK-2750 Ballerup, Denmark) was used with successful intubation. The position of the tracheal tube was verified with the bronchoscope. The tracheal tube was fixed, and the patient had the return of spontaneous circulation (ROSC). The next day, the patient was performing considerably better.

There was no fever, hypercapnia, or creatine phosphokinase (CPK) elevation. The patient continued to improve and was weaned from mechanical ventilation. She was discharged home without neurological deficits two weeks post-extubation.

**Final diagnosis:** Masseter muscle rigidity (MMR) by non-depolarizing neuromuscular blocking agent rocuronium.

**Discussion**

To the best of our knowledge, seven cases have been reported in the medical literature with masseter muscle rigidity (MMR) complication in non-depolarizing agents like rocuronium [2,3], vecuronium [4] and atracurium [5]. MMR almost always involves succinylcholine [6-9], a depolarizing agent [10]. MMR occurs with succinylcholine somewhere between 0.0001% to 0.1% of cases.

Malignant hyperthermia should be suspected in a patient with succinylcholine-induced MMR [11]. However, of the previous seven cases with non-depolarizing agents, malignant hyperthermia was found in only two cases.

There were isolated cases of masseter muscle rigidity without malignant hyperthermia in which supportive management is the only treatment like in this case [12,13].

When opening the jaw is a challenging situation, bag-mask ventilation should be used. Several maneuvers to handle MMR have been described, including laryngeal mask airway (LMA) insertion, bronchoscopy for nasotracheal intubation, fiberoptic scope devices attached to the blade of the laryngoscope, retrograde endotracheal intubation, and cricothyroidotomy [14]. Reports exist on the reversal of MMR with neostigmine and glycopyrrolate [15]. Propofol has been described as beneficial in case reports [16]. We found only one case of MMR with propofol that was attributed to the serotonin syndrome [17].

Sugammadex, a cyclodextrin, reverses rocuronium-induced neuromuscular blockade (NMB) [18]. The sugammadex molecule achieves this by encapsulating steroidal non-depolarizing neuromuscular-blocking agents (i.e. muscle relaxants) such as rocuronium and vecuronium, rendering the molecule inactive. Sugammadex is superior to the combination of neostigmine/glycopyrrolate in receiver operating characteristic (ROC) analysis for rocuronium. There are no cases reported on the use of sugammadex reversing rocuronium-induced MMR. However, sugammadex has successfully reversed the effects of non-depolarizing neuromuscular blocking agents in patients unable to be intubated or ventilated [19].

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Atracurium causes histamine release with a slower onset of action, thus it is not recommended for rapid sequence intubation. Rocuronium has an onset of action similar to succinylcholine (60 - 90 seconds), but the duration of the blockade is longer. Liver cirrhosis and chronic renal failure often result in an increased volume of distribution and a lower plasma concentration for a given dose of water-soluble drugs, such as muscle relaxants, but their clearance is prolonged requiring smaller maintenance doses. Vecuronium accumulates in renal failure due to partial excretion by the kidneys and possibly by its active 3-hydroxy metabolite [20].

Temporomandibular joint dysfunction mimics MMR. Immediate consideration must be given to treat the patient with muscle relaxants, and jaw manipulation. Fentanyl-induced jaw rigidity is accompanied by chest wall rigidity and is treated with naloxone [21]. The serotonin syndrome may cause rigidity; its treatment is the removal of the selective serotonin reuptake inhibitor (SSRI) drug. Other adverse reactions to neuromuscular blockade drugs are increased intraocular, intragastric pressure, and intracranial pressures. Other complications are rhabdomyolysis, hyperkalemia (succinylcholine), histamine release (atracurium), and anaphylaxis IgE mediated (1:10,000 - 1:20,000 anesthesias) [22].

Malignant hyperthermia (MH) has a genetic prevalence of 1:2000 cases, but reported cases varied between 1:5000 to 1:100 000. The disease was discovered in 1960 by anesthesiologist James Villiers, and published in 1962 in a patient with ten family members who died from anesthesia [23]. In the 1970s, cases triggered by halothane predominated. Over the past decade, sevoflurane has been the most common trigger, with isoflurane accounting for the greatest number of cases overall. Modern anesthetic techniques, as well as monitoring, has resulted in more indolent and insidious presentations [24,25]. Routine capnography has lead to early detection of MH, and withdrawal of triggering drugs. The clinical diagnosis is more doubtful; diagnosis may be delayed or missed in these times.

Malignant hyperthermia may be related to mutations in two genes: calcium voltage-gated channel subunit alpha1 S (CACNA1S) and ryanodine receptor 1 (RYR1). CACNA1S is present in 1% of the cases of MH. RYR1 is detected in 70% of the cases of MH with 31 variations identified thus far. This test is done in specialized centers for the diagnosis of MH as the first step in diagnosis. If the RYR1 mutation analysis is negative, then the caffeine halothane contracture test (CHCT) must be done by muscle biopsy if MH is still suspected [26].

RYR1 mutations may cause a dysfunctional calcium channel with the release of calcium from the sarcoplasmic reticulum causing a fatal hypermetabolic state. The calcium initiates the cross-linking of myofilaments in the cytosol, producing an intense muscle contraction with rigidity. The adenosine triphosphate (ATP) is consumed rapidly, causing a breakdown of the muscle membrane integrity, leading to rhabdomyolysis. Rhabdomyolysis elevates potassium, myoglobin, and creatine phosphokinase levels in circulation. The hypermetabolism produces high lactic acid levels due to fast oxygen consumption, increasing in PaCO₂ > 60 mmHg (detected mostly with capnography), fever rising initially by 1°C during the first 15 minutes, and later peaks to more than 40°C [27-30].

MH antidote is dantrolene, a ryanodine receptor antagonist that inhibits the release of calcium from the sarcoplasmic reticulum, but not the uptake of calcium [31]. Before the introduction of dantrolene in 1975, the mortality of MH was 70 - 80%, and now the mortality is less than 5% [30,32,33].

Hypersensitivity reactions to anesthesia agents are Immunoglobulin E (IgE) mediated and are estimated between 1:10 000 to 1:20 000 anesthesias. NMB agents represent the most frequently involved drug class with a range of 50-70% of hypersensitivity reactions overall. There is no systematic preoperative screening documented advice in the general population at this time. Other adverse effects are succinylcholine-triggered cytotoxic effects on muscle cells which are easy to distinguish from anaphylactic reactions [22].
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Conclusion

During a rapid sequence intubation, if difficulties arise, consider adverse reactions to NMB agents. Masseter muscle rigidity could be due to malignant hyperthermia or an isolated event. Investigation of malignant hyperthermia should be performed by family history, pertinent laboratories and appropriate genetic testing in this situation. Neostigmine/glycopyrrolate combination should be considered to reverse the masseter muscle rigidity during the administration of NMB agents including the depolarizing and the non-depolarizing ones.

Bibliography

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