Clinical Case Report

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Clinically suspected anaphylaxis induced by sugammadex in a patient with Weaver syndrome undergoing restrictive mammoplasty surgery

A case report with the literature review

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Abstract

Rationale: Sugammadex is a cylodextrin derivate that encapsulates steroidal neuromuscular blocker agents and is reported as a safe and well-tolerated drug. In this case report, we present a patient who developed grade 3 anaphylaxis just after sugammadex administration.

Patient concerns: A 22-year-old woman with diagnosis of Weaver syndrome was scheduled for bilateral mammoplasty and resection of unilateral accessory breast tissue resection. Anesthesia was induced and maintained by propofol, rocuronium, and remifentanil. At the end of the operation, sugammadex was administered and resulted in initially hypotension and bradycardia then the situation worsened by premature ventricular contraction and bigeminy with tachycardia, bronchospasm, and hypoxia.

Diagnosis: The Ring and Messmer clinical severity scale grade 3 anaphylactic reaction occurred just after sugammadex injection and the patient developed prolonged hypotension with recurrent cardiac arrhythmias in postoperative 12 hours.

Interventions: Treatment was initiated bolus injections of ephedrine, epinephrine, lidocaine, steroids and antihistaminic and continued with lidocaine bolus dosages and norepinephrine infusion for the postoperative period.

Outcomes: The general condition of the patient improved to normal 3 hours after the sugammadex injection, and she was moved to the intensive care unit. At 2nd and 8th hours of intensive care unit follow-up, she developed premature ventricular contraction and bigeminy with the heart rate of 130 to 135 beats/min, which returned to sinus rhythm with 50 mg lidocaine. After that, no symptoms were observed and the patient was discharged to plastic surgery clinic at the following day.

Lessons: Sugammadex may result in life-treating anaphylactic reaction even in a patient who did not previously expose to drug. Moreover, prolonged cardiovascular collapse and cardiac arrhythmias may occur.

Abbreviations: BP = blood pressure, ICU = intensive care unit, NMB = neuromuscular blocker.

Keywords: anaphylaxis, arrhythmia, hypotension, sugammadex

1. Introduction

Neuromuscular blocker (NMB) agents are used for the tracheal intubation and improvement of surgical conditions during the anesthesia induction and management. However, NMB agents are associated with residual neuromuscular blockade with the incidence of 20% to 60% during the early postoperative period.[1,2] This situation is associated with postoperative pulmonary complications like hypoxemia, pneumonia, and atelectasis needing reintubation which results in prolonged hospital stay and may be compelling in difficult airway cases.[3] Therefore, neuromuscular blockage is reversed before the extubation of the patient. Conventionally acetylcholinesterase inhibitors such as neostigmine is administered to the patients at the end of the surgery but neostigmine has nicotinic and muscarinic side effects and is reported to be associated with increased risk of postoperative hypoxia, atelectasis, and reintubation.[4–6]

Sugammadex is a synthetic cyclodexrin derivative that specifically removes steroidal neuromuscular blocking agent molecule.[7] It encapsulates the rocuronium as inclusion complex therefore it promptly reverses even deep of neuromuscular block preventing residual neuromuscular blockade and related respiratory complications. Sugammadex is biologically inactive, it does not bind to plasma proteins and many studies reported that it is safe and well tolerated.[7,8] Beyond these advantages, there are concerns that sugammadex is related to coagulation disorders and hypersensitivity reactions.[9,10]

Weaver syndrome is a rare disease of unknown etiology characterized by skeletal overgrowth, differential craniofacial, and digital anomalies and advanced bone age. Craniofacial anomalies present in these patients can cause intubation difficulty. There is no any data showing an association between Weaver syndrome and hypersensitivity reactions in the literature review.

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In this report, we aimed to present a case that developed anaphylaxis following sugammadex administration in a patient with Weaver syndrome undergoing reduction mammoplasty surgery. This case is different from other sugammadex-related hypersensitivity reactions because prolonged hypotension and recurrent cardiac arrhythmia attacks occurred during follow-up the intensive care unit (ICU). Written consent was obtained from the patient to publish this case report.

2. Case

A 22-year-old, 85 kg, 213 cm, female patient with Weaver syndrome diagnosis was scheduled for elective bilateral reduction mammoplasty resection of unilateral accessory breast tissue resection surgery. Her medical history is remarkable showing Weaver syndrome clinical findings including, overgrowth, macrocephaly, large hands and feet, developmental delay, controlled seizures, and vision problems. She had vitamin B allergy and underwent atrial septal defect and scoliosis surgeries with the anamnesis of difficult intubation. She was under regular follow-up with an endocrinologist and orthopedic surgeons. Macrocephaly, long philtrum, retrognathia, large ears, hypertelorism, high body lower extremity ratio, balance disorder, and scoliosis were detected on physical examination. There were no specific findings on preoperative laboratory tests and electrocardiogram. Patient characteristics are summarized in Table 1.

On the day of surgery, she was admitted to the operating room after premedication with 2 mg dormicum. She had the routine anesthesia monitoring with noninvasive blood pressure measurement, electrocardiogram, and peripheral oxygen saturation. Baseline blood pressure, heart rate, and oxygen saturation were 128/60 mm Hg, 75 beats/min, and 100%, respectively. General anesthesia was induced with 200 mg 1% propofol with 40 mg of lidocaine and continuous infusion of 0.3 μg/kg/min remifentanil after preoxygenation with 80% oxygen after preparation for difficult airway. Rocuronium 50 mg was injected intravenously for the facilitation of tracheal intubation. Endotracheal intubation was managed at the second attempt using videolanringoscope and gum elastic bougie with 9 mm cuffed endotracheal tube. Anesthesia maintenance was provided with propofol (6–8 mg/kg/h) and remifentanil (0.1–0.2 μg/kg/min) infusions. After intubation, cefazoline 1 g, as a prophylactic antibiotic, was administered intravenously. Mechanical ventilation set using volume control mode with tidal volume of 7 mL/kg and FiO_2 0.4. The surgery was uneventful for 7 hours.

At the end of the surgery, 340 mg IV sugammadex was administered to antagonize the residual neuromuscular block. Immediately after sugammadex administration, heart rate decreased from 72 to 43 beats per minutes and the blood pressure (BP) decreased from 125/65 to 43/25 mm Hg. Immediately, 10 mg IV ephedrine was administered and followed by rapid infusion of lactated Ringer's solution. However, the BP was still 51/23 mm Hg and premature ventricular contraction and bigeminy with the heart rate of 125 beats/min occurred. After immediate administration of intravenous 50-μg epinephrine and 60 mg of lidocaine, rhythm returned to sinus rhythm and BP increased to 80/60 mm Hg. Invasive BP monitoring was established in the right-radial artery and her arterial blood gas tests showed increased hemoglobin and hematocrit levels. Her face and upper body were flushed; the airway pressure showed an elevation and bronchospasm was diagnosed by revealing wheezing. Her peripheral oxygen saturation was 86% and BP decreased again to 57/32 mm Hg. Sugammadex related anaphylaxis is suspected and 50-μg epinephrine injection was repeated, methylprednisolone 125 mg, famotidine 20 mg, and pheniramine maleat were injected and continuous infusion of nor-epinephrine was started at the rate of 0.04 μg/kg/min, and her BP was stabilized at 90/50 mm Hg. Three hours after sugammadex administration the patient was extubated when no further bronchospasm or wheezing and transferred to ICU. She developed premature ventricular contraction and bigeminy with the heart rate of 130–135 beats/min, which returned to sinus rhythm with 50 mg lidocaine 2 hours and 8 hours after ICU accepted. She continued to receive 0.02 μg/kg/min norepinephrine for the stabilization of the mean arterial pressure at 60 mm Hg until the postoperative 12 hours and she discharged from ICU to the plastic surgery department 24 hours after the operation. In the ICU, she underwent cardiology consultation, blood cardiac enzymes levels, and transthoracic echocardiographic evaluations were normal. Clinical details of the patient related to anaphylaxis are given in Table 2. Results of blood gas analysis, serum Ig E, and tryptase levels assessed 3 and 24 hours after the onset of anaphylactic reaction were within the normal range (Table 3). On postoperative day 7, she discharged to home with normal ECG

Table 1

Patient characteristics.

Age	22
Sex	Female
Weight, kg	85
Height, cm	213
Operation	Bilateral reduction mammoplasty Resection of unilateral accessory breast tissue resection
Medical history	Weaver syndrome Atrial septal defect and scoliosis surgeries
Allergy history	Vitamin B

Table 2

Clinical details of the patient related to anaphylaxis.

Previous exposure to sugammadex	No
Symptoms	Bradycardia: 43 bpm Hypotension: 43/25 mm Hg Arrhythmia: PVC with bigeminy and tachycardia Facial and truncal flushing Decreased SpO_2: 86% Elevated airway pressure: 40 cmH_2O
Duration between sugammadex injection and	
• CVS signs	<1 minutes
• Respiratory signs	5 minutes
• Skin-mucosal tissue signs	5 minutes
• Sugammadex dosage	4 mg/kg
Treatment	Ephedrine 10 mg IV Epinephrine 50 μg IV Lidocaine 60 mg IV Methylprednisolone 125 mg IV Famotidine 20 mg IV Pheniramine maleat 45.5 mg IV Nor-epinephrine 0.04 μg/kg/min IV infusion
Duration between treatment initiation and hemodynamic stability	12 hours
Biphasic reaction	Arrhythmia: PVC with bigeminy and tachycardia

CVS = cardiovascular signs, PVC = premature ventricular contraction, SpO_2 = peripheral oxygen saturation.

Table 3

Results of the diagnostic tests.

	Serum tryptase, ng/mL		Total Ig E, kU/L	
	Result	Reference range	Result	Reference range
3 hours after sugammadex	7.64	<11.5	7.54	0.00–87.00
12 hours after sugammadex	1.80	<11.5	6.69	0.00–87.00

and laboratory tests but refused to have further skin tests for definitive diagnosis.

3. Discussion

Perioperative anaphylaxis is a rare but life-treating clinical condition involving multiply organ systems. Skin, mucous membranes, cardiovascular, respiratory systems, and gastrointestinal systems are the most involved target organs. The Ring and Messmer clinical severity scale reported that erythema, edema, pruritus, hypotension, bradycardia, tachycardia, and bronchospasm are the corresponding clinical signs of perioperative anaphylaxis.[11] The World Allergy Organization published a guideline corresponded to the diagnosis of anaphylaxis and it was reported that perioperative anaphylaxis mostly occur a few minutes after intravenous administration of causative agent (Table 4).[12] Neuromuscular blocking drugs, latex, and antibiotics are the most common causes of perioperative anaphylaxis.[13]

A gamma cylodextrin derivate sugammadex, which was designed to reverse rocuronium-induced neuromuscular block is also reported to cause hypersensitivity reactions. Godai et al[14] reported 3 cases with suspected allergic reaction of different degrees of severity occurred after sugammadex administration. In contrast, Kawano et al[15] reported a case in which sugammadex was used to treat an anaphylactic reaction that occurred after rocuronium is presented.

The first line of the diagnosis of perioperative anaphylaxis includes clinical features, severity of clinical signs, and the interval between the causative agent and onset of clinic features. According to the World Allergy Organization guideline, anaphylaxis was diagnosed when any of the 3 criteria in Table 4 were fulfilled. In the present case, anaphylaxis was clinically diagnosed based on this guideline and according to the Ring and Messmer 4 step grading scale of anaphylaxis; the intensity of reaction was grade 3 with life-treating clinic features including hypotension, tachycardia, cardiac arrhythmia, bronchospasm, and hypoxia. In this case, the anaphylaxis signs occurred immediately after sugammadex administration suggesting the sugammadex as a causative agent. However, we are unable to evidence this case with the specific diagnostic laboratory findings of anaphylaxis. Tryptase and Ig E levels of the present patient were within normal ranges and the skin prick test did not applied to the patient. Elevated Htc and Hb levels in the first 3 hours were our only anaphylaxis supporting laboratory findings.

Miyazaki et al[16] just reported a retrospective investigation regarding anaphylaxis associated with sugammadex. Their results showed that 6 patients among 15,479 sugammadex administered patients developed anaphylaxis. All the reported patients recovered without major problems and biphasic reactions. In all of the patients anaphylaxis symptoms occurred within the 5 minutes of sugammadex administration and hemodynamic stability was achieved in the first 30 minutes and anaphylaxis diagnosis was confirmed with laboratory only in 1 patient. In this patient, the anaphylaxis clinic occurred immediately after suggamadex injection; moreover, the patient needed norepinephrine infusion to maintain blood pressure and showed biphasic reaction with recurrent cardiac arrhythmias.

In summary, we report a case of clinically suspected anaphylaxis reaction in a patient who received sugammadex at a dose of 4 mg/kg. The reaction, occurred just after sugammadex administration, it was severe, had biphasic character, and needed prolonged norepinephrine infusion. This case report is important to take attention to the hypersensitivity reactions regarding sugammadex which may be life treating with life treating and prolonged hypotension combined with recurrent arrhythmias.

Table 4

Clinical criteria for diagnosing anaphylaxis adapted from world allergy organization guidelines.

1. Acute onset of illness with involvement of the skin, mucosal tissue, or both (generalized urticaria, itching, or flushing) and at least 1 of the following:
   A. Respiratory compromise (dyspnea, wheeze, bronchospasm, stridor, or hypoxemia)
   B. Reduced blood pressure or associated symptoms of end-organ dysfunction (hypotonia, syncope, or incontinence)
2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient:
   A. Involvement of the skin-mucosal tissue (generalized urticaria, itching, or flushing)
   B. Respiratory compromise (dyspnea, wheeze, bronchospasm, stridor, or hypoxemia)
   C. Reduced blood pressure or associated symptoms (hypotonia, syncope, or incontinence)
   D. Persistent gastrointestinal symptoms (crampy abdominal pain or vomiting)
3. Reduced blood pressure after exposure to known allergen for that patient:
   A. Adults: systolic blood pressure of <90 mm Hg or >30% decrease from that patient's baseline

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