



Case report

Anaphylaxis to vecuronium: the use of basophil CD63 expression as a possible screening tool to identify a safe alternative

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Abstract A 29-year-old woman with a history of anaphylaxis during anesthesia required diagnostic laparoscopic surgery for investigation of infertility. Previous laboratory investigations suggested that she had reacted to vecuronium, but she also had a specific IgE antibody to succinylcholine. The use of the basophil activation marker CD63 as a screening tool in selecting a safe muscle relaxant is presented.
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1. Introduction

Anaphylaxis in the perioperative period is associated with morbidity and mortality, and it also has implications for each patient for any future surgery [1]. Most anesthesiologists rarely encounter anaphylaxis, and there can be great difficulty in making a diagnosis. Even more difficult than making the primary diagnosis is the identification of the responsible drug. Neuromuscular blocking drugs are the most frequently implicated in anaphylaxis, with cross-reactivity between drugs as high as 63.4% [2]. The usefulness of the basophil activation marker CD63 [3] in selecting a safe muscle relaxant for a patient who had had a previous anaphylactic reaction to vecuronium and also showed cross-sensitivity to succinylcholine is presented.

Written informed consent for publication of this case report was obtained from the patient.

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2. Case report

A 29-year-old woman with a history of anaphylaxis during anesthesia required diagnostic laparoscopic surgery for investigation of infertility. Given her history of a previous anaphylactic reaction to vecuronium and her cross-sensitivity to succinylcholine, she was referred to an anesthesiologist for consultation. She had been anesthetized in 1998 for a similar procedure (laparoscopy and tubal dye test). Anesthesia had been induced with fentanyl and propofol, with vecuronium administered to facilitate tracheal intubation. The patient's trachea was intubated uneventfully, but within 2 min, she had become flushed and profoundly hypotensive (systolic blood pressure, 69 mm Hg) with a peripheral oxygen saturation of 84%. She was successfully resuscitated with intravenous fluids, ephedrine, hydrocortisone, and chlorpheniramine; surgery was cancelled.

Three samples of blood had been taken for tryptase measurement, one immediately after resuscitation, one at 6 h, and one 24 h later. The tryptase levels were 117, 57, and 12

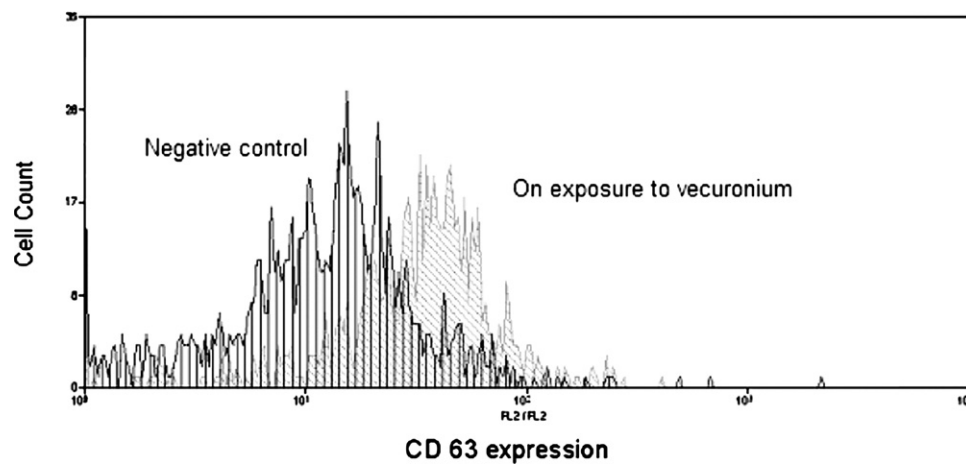


Fig. 1 Example of a positive result when basophils are exposed to vecuronium 0.01 mg/mL compared with a negative control (phosphate buffer saline).

(normal, $<13.5 \mu\text{g/L}$), respectively, showing clear evidence of mast cell activation. Blood also had been taken for specific IgE assays. There is no readily available test for specific IgE against vecuronium. The specific IgE for succinylcholine was found to be positive and of grade 3 (moderate) reactivity. Total IgE was 755 kU/L (normal, <81). Skin prick tests were performed for fentanyl and propofol at serial log dilutions from 1:1000 to neat. These tests were all negative.

Given the patient's history, the safest anesthetic choice would have been general anesthesia without the use of a muscle relaxant, or regional anesthesia. However, given the patient's body mass index of 33 kg/m^2 , steep Trendelenburg positioning, and the need for a pneumoperitoneum, it was felt that optimal laparoscopic surgical conditions could be achieved only with general anesthesia and muscle paralysis.

It is normal practice in our hospital for patients with a history of perioperative anaphylaxis to be seen by a consultant anesthesiologist and a consultant immunologist. The cases are reviewed, and an investigative strategy for identifying trigger agents and an anesthetic plan are decided jointly. It was decided to investigate basophil activation to the commonly used neuromuscular blocking drugs (succinylcholine, vecuronium, and cisatracurium). Basophil activation tests using changes in cell phenotype CD63 have been used previously to diagnose reactivity to various drugs, including neuromuscular blocking drugs [3]. The following were concentrations of the drugs used for the basophil activation tests: vecuronium—0.002, 0.02, and 0.2 mg/mL; succinylcholine—0.05, 0.5, and 5 mg/mL; and cisatracurium—0.002, 0.02, and 0.2 mg/mL. The tests were positive for succinylcholine and vecuronium, and negative for cisatracurium. A basophil activation test was considered positive if more than two dilutions of a drug produced more than 10% basophil activation. The patient also was found to have a positive reaction to skin prick testing with vecuronium (0.2 mg/mL) (Fig. 1).

It was felt that cisatracurium should be used as the neuromuscular blocking agent. The patient was admitted to

the hospital on the night before the operation. The results of the immunological testing were explained to the patient. She was given promethazine 50 mg, ranitidine 150 mg, and dexamethasone 1 mg the night before surgery, and promethazine and ranitidine were repeated on the morning of surgery. Dexamethasone was chosen because of its high glucocorticoid (anti-inflammatory) activity and insignificant mineralocorticoid activity. It was given in a dose equivalent to 25 mg of hydrocortisone. Anesthesia was induced with fentanyl 100 μg , propofol 200 mg, and neuromuscular block was established with cisatracurium 12 mg. Analgesia was provided with diclofenac 100 mg per rectum together with 0.5% bupivacaine subcutaneous infiltration of the incisions. Anesthesia was maintained with sevoflurane in an air-oxygen mixture, and surgery proceeded uneventfully.

3. Discussion

When a patient is identified as having had an anaphylactic reaction to a previous anesthetic agent, it causes considerable concern to both the patient and anesthesiologist. Cross-reactivity between neuromuscular blocking drugs is significant, and the main antigenic determinants are thought to be the quaternary ammonium groups that are capable of bridging IgE antibodies [4].

There are a number of tests for the diagnosis of anaphylactic reactions. Some of these tests, such as plasma tryptase, are done at the time of the event and lend support to the diagnosis of anaphylaxis. Other tests such as skin prick tests, which are completed later, may help to identify the drug in question. The significance and interpretation of laboratory and skin tests have been the subject of much debate in the literature [5-7]. Basophil activation studies using mediator (histamine and leukotrienes) release also have been used previously to show clinical allergy [8]. Flow cytometry analysis of cell expression using basophil

activation markers such as CD63 and CD203c is gaining increasing popularity [9-11]. When basophils degranulate in an anaphylactic response, these transmembrane proteins are expressed in greater amounts on the basophil cell surface membrane. Recent published literature examining the effectiveness of these markers in latex allergy [11] and other common allergies [10-13] has shown promising results. Monneret et al [3] reported the usefulness of CD63 expression in the investigation of allergy to neuromuscular blocking drugs, and more recently, Sudheer et al [14] studied the use of CD63 and CD203c in the investigation of perianesthetic anaphylaxis. The sensitivity of CD63 in various studies range from 54% to 79%, and the specificity, from 93% to 100%. The usefulness of CD203c is less satisfactory. In one study investigating muscle relaxant allergy, the sensitivity was 36%, but the specificity 100%. The perioperative use of histamine antagonists and steroids in those patients thought to be at risk is encouraged. Both mast cells and basophils are known to release proteases and histamine. However, no specific pretreatment reliably prevents anaphylaxis [15].

It is critical not only to render a diagnosis but also to identify the offending drug. Neuromuscular blockers have a high cross-reactivity, and thus, it is also important to know which alternate drug can be administered safely. New in vitro tests such as examining phenotype changes on basophils might be helpful.

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