

A case of perioperative allergic reaction caused by rocuronium and atropine



Michiyo Nakagawa, MD, PhD, Miho Hanada, MD, and Hiroo Amano, MD, PhD
Yababa-cho, Japan

Key words: atropine; cross-reactivity; perioperative allergy; rocuronium; tropic acid.

INTRODUCTION

Perioperative allergy is rarely encountered, but its causative agents have been reported to include neuromuscular blocking agents (NMBAs), latex, and antibiotics. Although atropine is used widely as an anticholinergic agent, a type I allergy or anaphylaxis associated with atropine has rarely been reported. Here, we report a rare case of an allergic reaction to atropine and rocuronium at the time of the first general anesthesia in a patient with no history of exposure to either agent. We also discuss the sensitization pathway involved.

CASE REPORT

An 11-year-old Japanese boy was referred to our department because urticaria developed all over his body immediately after receiving an injection of 1 g cefmetazole sodium, 0.25 mg atropine, 50 mg propofol, and 30 mg rocuronium during the induction of anesthesia to undergo an appendectomy. There were no marked changes in his vital signs. After he received methylprednisolone, his urticaria disappeared, and the surgery was completed successfully. No disinfectant had been used before the appearance of urticaria. His medical history included sties, conjunctivitis, and upper left scleritis. He had no history of surgery or allergies. The results of an ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden) test showed that IgE specific for Latex and Hev b 6.02 was absent. We suspected an allergy to 1 or more of the drugs injected during the induction of anesthesia. A skin prick test and an intradermal test (IDT) were performed 11 weeks after the development of the allergic reaction to determine the cause of the allergy. We first performed the skin prick test.

Abbreviations used:

IDT: intradermal test
NMBAs: neuromuscular blocking agents

It was performed using the prick-prick method, and a positive result was considered when the average wheal diameter induced by the allergen was 50% of the positive control response induced by histamine chloride at 10 mg/mL. We tested undiluted cefmetazole sodium, atropine, propofol, and rocuronium; the results were all negative. Then, we carried out IDT with the same reagents. IDT was started at a 1/100 dilution of the stock solution, followed by a 1/10 dilution. IDT included the injecting 0.02 mL of a diluted solution into the dermis, with the results evaluated 15 minutes later. A standardized read-out system for IDT has not been developed, but an IDT result is normally considered positive when the diameter of the wheal is double the length of the initial papule and surrounded by a typical flare.¹ Positive reactions were observed to rocuronium (1/10 dilution), rocuronium (1/100 dilution), and atropine (1/10 dilution) (Table 1). Negative reactions were observed to propofol, cefmetazole sodium (1/100 and 1/10 dilutions), and atropine (1/100 dilution) (Table 1). Based on these findings, we diagnosed him with an immediate allergic reaction to rocuronium and atropine.

DISCUSSION

Atropine is an anticholinergic agent, with a structural formula consisting of tropine and tropic acid. It is used as a premedication for anesthesia

From the Department of Dermatology, School of Medicine, Iwate Medical University, Yahaba-cho.

Funding sources: None.

Conflicts of interest: None disclosed.

IRB approval status: Not applicable.

Correspondence to: Michiyo Nakagawa, MD, Department of Dermatology, Iwate Medical University, 2-1-1 Idaidori, Yahaba-cho, Shiwa-gun, Iwate 028-3695, Japan. E-mail: mnakagaw@iwate-med.ac.jp and hamano@iwate-med.ac.jp.

JAAD Case Reports 2021;7:84-6.
2352-5126

© 2020 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.jidcr.2020.11.009>

Table I. Results of IDT. Positive reactions were observed to rocuronium (1/10 dilution), rocuronium (1/100 dilution), and atropine (1/10 dilution). Negative reactions were observed to propofol, cefmetazole sodium (1/100 dilution and 1/10 dilution), and atropine (1/100 dilution)

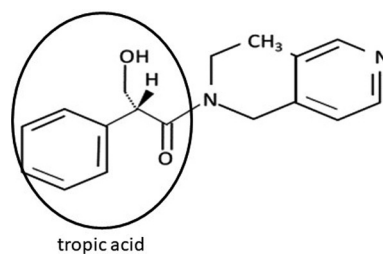
Allergen	Wheal (mm)	Erythema (mm)
Rocuronium 1/100 dilution	5 × 5	15 × 10
Atropine 1/100 dilution	3 × 3	0 × 0
Propofol 1/100 dilution	0 × 0	0 × 0
Cefmetazole sodium 1/100 dilution	0 × 0	0 × 0
Rocuronium 1/10 dilution	10 × 8	21 × 10
Atropine 1/10 dilution	4 × 3	13 × 9
Propofol 1/10 dilution	0 × 0	0 × 0
Cefmetazole sodium 1/10 dilution	0 × 0	0 × 0
Saline	0 × 0	0 × 0

IDT, Intradermal test.

due to its gland secretion inhibitory action. Atropine allergy is rare, and only 5 cases have been reported to date.²⁻⁶ All 5 cases occurred in adults due to anesthesia administered for a surgery and manifested immediately after the administration. The symptoms varied and included skin symptoms, digestive symptoms, respiratory symptoms, and hypotension. In 1 case, the sensitization route of atropine was presumed to be a previous surgery.³ However, our case had no history of surgery or atropine administration. He had undergone ophthalmologic treatment in the past. At the time, he had received tropicamide drops. Tropicamide results in ophthalmologic mydriasis and paralysis, which are useful for diagnosis or treatment. Both tropicamide and atropine have the same tropic acid derivative structure. Sensitization to the tropic acid structure of tropicamide may have thus caused a cross reaction with atropine. These agents have common structures (Fig 1).

All Japanese NMBA have quaternary ammonium ions. Structure-activity studies have been performed to explore the molecular basis of specific IgE binding. These studies have established that quaternary and tertiary ammonium ions are the main components of allergenic sites in reactive drugs.⁷ Another intriguing aspect of allergic reactions to NMBA concerns the dogma of a previous exposure. Many reactions are reported after the first known contact with an NMBA.⁸ This quaternary ammonium ion structure is commonly found as a surfactant in everyday products, such as toothpaste, shampoo, cosmetics, bleach, and antitussives.^{7,8} Patients who have never used NMBA but develop anaphylaxis after the very first dose may have been sensitized by a cross reaction with quaternary ammonium ion

tropicamide



atropine

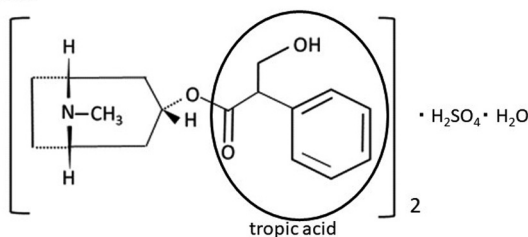


Fig 1. Both tropicamide and atropine have the same tropic acid derivative structure. Tropicamide's and atropine's common component is circled. Chemical formulae are provided with permission from the Ministry of Health, Labor and Welfare of Japan. According to the Ministry, which handles the Japanese Pharmacopoeia, the content can be reproduced freely. Source: Ministry of Health, Labor and Welfare website: <https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000066530.html>

compounds.⁹ We instructed the patient to carry a drug allergy card and provided him with a list of quaternary ammonium ion-free products. Until now, he has experienced no symptoms despite using quaternary ammonium ion-containing products. Therefore, his product use is not restricted.

He had never used rocuronium or atropine. The atropine-induced allergic reactions may have been caused by cross reactivity of the tropic acid structure of tropicamide. The allergic reactions to rocuronium were thought to be due to a cross reaction with quaternary ammonium ion compounds, which are common sensitizers.

REFERENCES

- Jensen CB. Intracutaneous (or Intradermal) test. In: Skin Test for Immediate Hypersensitivity. In: Johansen JD, Frosch PJ, Lepoittevin JP, eds. *Contact Dermatitis*. 5th ed. Berlin: Springer; 2011:515.
- Choi J, Kim H, Jeon Y-S, Hong DM. Anaphylaxis following atropine administration during general anesthesia: a case report. *Korean J Anesthesiol*. 2015;68(5):496-500.
- Coelho D, Fernandes T, Branga P, Malheiro D, Rodrigues J. Intraoperative anaphylaxis after intravenous atropine. *Eur J Anaesthesiol*. 2007;24(3):289-290.
- Aguilera L, Martinez-Bourio R, Cid C, Arino JJ, Saez de Eguilaz JL, Arizaga A. Anaphylactic reaction after atropine. *Anaesthesia*. 1988;43(11):955-957.

5. Obara Y, Konakawa A, Ishii K, et al. [A case of immediate allergic reaction caused by atropine during induction of anesthesia]. *Kanagawa Igakukai Zasshi*. 2013;40(2):178 (in Japanese).
6. Arai M, Tomozuka N, Yamada Y, et al. [A case of anaphylactic shock due to intraoperative atropine administration]. *Masui*. 2005;54(5):571 (in Japanese).
7. Baldo BA, Fisher MM. Substituted ammonium ions as allergenic determinants in drug allergy. *Nature*. 1983;306(5940):262-264.
8. Mertes PM, Alla F, Tréchet P, Auroy Y, Jouglu E, des Réactions Anaphylactoides GD. Anaphylaxis during anesthesia in France: an 8-year national survey. *J Allergy Clin Immunol*. 2011;128(2):366-373.
9. Mertes PM, Tajima K, Regnier-Kimmoun MA, et al. Perioperative Anaphylaxis. *Med Clin North Am*. 2010;94(4):761-789.