



Local allergic reaction to atracurium besylate: an uncommon and unique reason

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Abstract

Allergy to muscle relaxants is a known entity. Several drugs can be incriminating for both major and minor allergic reactions in the perioperative setting. These reactions are either of immunologic origin (IgE mediated anaphylaxis) or related to direct stimulation of histamine release (anaphylactoid reactions). Atracurium besylate, an intermediate acting non-depolarizing neuromuscular blocking agent (NMBA), belonging to the tetrahydroisoquinolinium class, is associated with allergic reactions, including severe anaphylaxis. We present a unique mechanism (the tourniquet effect of a blood pressure cuff) for local cutaneous allergy to intravenous atracurium in a breast cancer patient, which is further reinforced by postoperative allergologic work-up. Eternal vigilance and high degree of suspicion are advocated to diagnose and manage such reactions.

Keywords: Allergy, histamine, neuromuscular blocker, atracurium besylate, allergologic work-up, tourniquet effect, local reaction

Introduction

Neuromuscular blocking agents have been associated with allergic reactions since time immemorial. Atracurium besylate can cause a variety of allergies. Blood pressure cuffs are routinely applied around the upper arm and frequent readings are taken under anesthesia, especially during induction. We describe a peculiar allergic reaction to atracurium when administered to a breast cancer patient in the same arm as the cuff and cannula.

Case presentaion

An ASA grade 1, 40 year old female patient was posted for right sided modified radical mastectomy (MRM) for carcinoma of right breast. She also had history of surgery and deformity of the right upper extremity. She had no other co-morbidities and no history of any drug allergies. Her previous surgery and anesthesia were uneventful, done under general anesthesia (TIVA-total intravenous regional anesthesia without muscle relaxants under spontaneous respiration and laryngeal mask airway) with regional block. Since MRM was to be done on right breast, intravenous (I.V.) cannula was taken on the left hand. Since right arm was previously operated upon, blood pressure (B.P.) cuff for non-invasive B.P. monitoring was wrapped around the left arm. In our institution, it is a routine practice to measure the B.P. every 1 minute during induction of general anesthesia

(GA), along with continuous ECG (electrocardiogram), Pulse, Temperature, End-tidal Carbon-dioxide concentrations and Oxygen saturation monitoring. Intravenous induction of GA was done with Midazolam 2mg, Fentanyl citrate 80microgram and Propofol 80mg. After loss of eye lash reflex and confirming bag-mask ventilation, intravenous Atracurium besylate (a non-depolarising NMBA–neuromuscular blocking agent) 40mg was given slow I.V. Within 1 minute of atracurium injection, the patient developed local erythema, cutaneous wheal and prominence of hair follicles in the area between the intravenous cannula and the lower rim of the B.P. cuff (**Figures 1 and 2**). The vital parameters were stable, with no increase in heart rate or fall in B.P. The chest was clear on auscultation and there were no signs of allergy anywhere else. After routine endotracheal intubation with a cuffed tube, the airway pressures were found to be normal and the hemodynamic status was maintained. There was no evidence of bronchoconstriction or laryngospasm or cardiovascular collapse in the entire perioperative period. Intravenous hydrocortisone, dexamethasone and diphenhydramine were given to ameliorate this allergic reaction. There were no generalized reactions even after B.P. cuff deflation. Atracurium was not repeated after the allergic reaction and further NMBA top-ups were given with Vecuronium bromide, an intermediate acting neuromuscular blocking agent. Vecuronium



Figure 1. Photo of the left forearm between the intravenous cannula and the lower rim of blood pressure cuff showing cutaneous wheals and erythema.



Figure 2. Close-up photo of the local allergic reaction after Atracurium injection.

was given slowly forty minutes after the first dose of atracurium under neuromuscular monitoring (used routinely for all cases needing muscle relaxants in our institution) and it did not cause any aggravation of previous reaction or any

fresh allergy. The size of the cutaneous wheals and intensity of erythema diminished with time and disappeared spontaneously a few minutes after extubation. Careful watch for any serious allergic reaction or anaphylaxis was done both intraoperatively and postoperatively. On detailed questioning, the patient gave history of cough medication ingestion for dry cough, pholcodeine syrup for one week, several days prior to the present surgery. Skin allergy testing was done in the onco-surgical intensive care unit (ICU) with all preparations for resuscitation, in the event of any serious reactions. Intradermal testing using 0.03ml of 1 microgram/milliliter concentration (1/1000 dilutions) of atracurium was done to raise a just discernable bleb on the inner volar surface of the other forearm. A persistent wheal 1cm in size developed after about 7 minutes and this did not further increase in size at 20 minutes after injection when the test was interpreted. The control wheal did not increase in size from the initial 1mm size. Testing with vecuronium at a concentration of 400 microgram/ml resulted in only a 0.2 cm wheal. The patient was monitored and observed in the ICU for 24 hours and then shifted out after an uneventful course. The blood pressure cuff was wrapped around the thigh in the postop ICU.

Discussion

The incidence of hypersensitivity reactions during anesthesia is reported to be 1:1250 to 1:13000 anesthetics [1]. Such reactions can be either allergic or non-allergic. Allergic reactions can be either IgE mediated or non-IgE mediated. Out of the drugs incriminated, neuromuscular muscular blocking agents (NMBA's) are the most prone to cause allergic reactions. Benzyl-isoquinolines are more potent histamine releasers than aminosteroid NMBA's, which can be prevented by slow injection or pretreatment with anti-histamines. Our case highlights the fact that local allergic reaction to atracurium [2] can occur without any systemic manifestations. As the B.P. cuff and the intravenous cannula were on the same arm, the cutaneous allergy was evident only on the left upper extremity. When the B.P. cuff was inflated to measure the B.P. non-invasively every 1 minute, it acted as a tourniquet, impeding venous flow on the left arm. Hence, the features of allergic reaction were limited to the area between the I.V. cannula and the lower rim of the B.P. cuff. The tourniquet effect also increased the distal intravenous concentration of atracurium causing local allergic reactions. There were no allergic reactions to other induction agents administered I.V. before atracurium, as this patient also had no history of allergy to same intravenous agents administered during previous surgery on the right arm (conducted under TIVA with I.V. Propofol, Fentanyl and Midazolam). The patient did not receive any neuromuscular blocker during previous surgery. Atracurium can cause histamine release, more so on rapid I.V. injection [3]. We had injected atracurium slowly over 30 seconds. The manifestations of cutaneous allergy persisted till the time of the breast surgery, as the blood pressure

cuff was on the same arm as the I.V cannula. It disappeared postoperatively, where a larger B.P. cuff was wrapped around the thigh for blood pressure measurements. This reaction was not due to local vasodilation, as in that case it could have increased with vecuronium administration or occurred initially with Propofol administration, which has vasodilatory properties. Moreover, Atracurium undergoes quick Hoffmann degradation in the plasma and does not depend on organ metabolism for elimination. We had to continue with the surgery as the patient was hemodynamically stable, with no systemic manifestations and surgical relaxation was required for the breast and axillary lymph node dissection. Vecuronium was administered as the incidence of allergic reactions to it is lower and muscle relaxation was needed for the tumor dissection to be completed. Even though Vecuronium administration is not recommended in the absence of a specific investigation regarding a possible cross-sensitization, we still used it under vigilant monitoring and extensive precautions for resuscitation, as there was no other choice available to us at that critical juncture. Even though this could have acted retrospectively as a negative challenge test [4], it was not the reason for vecuronium administration. It was only given to tide over the need for surgical relaxation, as cancer surgery cannot be stalled in the middle, especially if the patient was hemodynamically stable and there are no systemic signs of allergy. Previous exposure to pholcodiene [5] could have caused the current sensitization to atracurium that subsided post-surgery without any complications. This sensitization was compounded by the tourniquet effect of the blood pressure cuff on the implicated arm. Quarternary ammonium ion is present in a large variety of foods, household chemicals and drugs. In our case, the patient had consumed pholcodeine-containing cough mixture, which is a known potent stimulator of IgE production. Hence, a first time NMBA exposure (as in our case), can also lead to hypersensitivity reactions due to prior sensitization to quaternary ammonium ions. No other anesthetic used during the previous surgery contained any quaternary ammonium group and there was no reported allergy during the previous anesthesia exposure. The same induction agents were administered during current surgery as well before atracurium, which did not result in any allergy (Propofol, Fentanyl and Midazolam). Hence, it was logical to suspect atracurium as the causative agent of the allergy, confirmed by allergologic workup.

Conclusions

A warning band was issued to the patient and a prominent note of allergy was made in the discharge summary. This type of purely local drug allergy due to tourniquet effect should also be kept in mind when dealing with quaternary ammonium compounds. Cutaneous intradermal sensitivity testing [6] for NMBA's done in the postoperative period showed that the patient was allergic to atracurium. We need to be extra cautious, both while administering drug as well as during testing,

as tetrahydroisoquinolinium class [7] of NMBA's are prone to cause allergic reactions. As Cis-Atracurium has the lowest risk of reaginic or non-reaginic reactions, its use is recommended. Unfortunately, it is not available in our institution and many other developing nations. Sometimes, allergic reactions are unique and do not follow textbook descriptions. Hence, it is also important to report and investigate such reactions for better patient safety and advancement of scientific research. Eternal vigilance with prompt treatment and future avoidance of the incriminating agent [8] is the key to successful patient outcome.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Authors' contributions	UH	SBS	AKB
Research concept and design	✓	--	✓
Collection and/or assembly of data	✓	✓	--
Data analysis and interpretation	✓	✓	--
Writing the article	✓	✓	✓
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