

Correspondence

A case of midazolam anaphylaxis during a pediatric patient's first anesthetic☆☆



Perioperative anaphylaxis remains a relatively rare (with an estimated incidence 1:3,500 to 1:20,000) but important cause of morbidity and mortality [1]. Common causes include neuromuscular blockers, antibiotics, and latex [1,2]. Diagnosis of perioperative anaphylaxis may be delayed, as general anesthesia may mask the characteristic symptoms of hypotension, rash, and airway swelling. Herein we present a case of midazolam anaphylaxis in a child's first anesthetic.

A 17 year-old, 87.2 kg, otherwise healthy male, with a history of Wolff-Parkinson-White, was scheduled to undergo EP ablation. He was given 2 mg IV of midazolam, induced with fentanyl, propofol, and vecuronium, endotracheally intubated, and maintained with sevoflurane and propofol. Prior to catheter placement, vecuronium was re-dosed. Ten minutes later, blood pressure suddenly decreased from 100/50 to 68/24 mm Hg and heart rate increased from 70 to 125 beats per minute. Small doses of pressors failed to restore blood pressure and pulses were not palpable. High-quality CPR was initiated and resuscitation continued with larger doses of epinephrine, CaCl₂, and IV fluid. Physical exam showed hives on the chest and face. Intraoperative transthoracic echocardiogram showed underfilled ventricles with normal function. Because of the timing of symptom-onset, an anaphylactoid/anaphylactic reaction to vecuronium was suspected. The patient's hemodynamics were stabilized with epinephrine and vasopressin drips. Despite 5 L of crystalloid (lactated ringers), his hematocrit was 51%. Serum tryptase drawn during the resuscitation and was markedly elevated at 31.7 µg/L (normal < 11.4) and returned to normal the next day. He recovered uneventfully and underwent formal skin and intradermal testing weeks later and was found to be reactive to midazolam alone.

In cases of suspected anaphylaxis, obtaining a serum tryptase level can be useful. Current literature recommends obtaining a level between 1 and 4 h after symptom onset [4,5]. Elevated tryptase levels can be seen in both IgE-mediated anaphylactic and anaphylactoid reactions, however a level > 25 µg/L is more suggestive of an anaphylactic reaction [3]. Skin testing is ideally undertaken 4–6 weeks after initial event, to allow histamine and other mediator levels to return to baseline. Sensitivity for skin testing is approximately 94–99% for NMBA's, and 75–90% for latex [5]. Due to the potential hassle for the patient and/or family, it might be tempting to forgo skin testing and list one of the most likely agents (Fig. 1) as the culprit. In fact, we initially listed vecuronium as the allergen, until skin testing was completed. Knowing that midazolam alone was the culprit had significant impact for this patient in regards to future anesthetics, especially as he returned later for his EP ablation.

Another interesting point from our case was the persistently elevated hematocrit, despite 5 L of crystalloid during resuscitation. It is well known that the inflammatory mediators released by an anaphylactic reaction can cause vasodilatation and increased vascular permeability, and a prior study reported as much as a 35% decrease in circulating blood volume within 10 min due to transfer of intravascular fluid to extravascular space [6]. The patient's persistently elevated hematocrit in this case was likely an indication of significant movement of fluids interstitially despite aggressive intravascular volume replacement.

Despite midazolam's widespread use in current anesthetic practice, severe anaphylaxis like this patient experienced especially with no prior anesthetics or history of prior allergies/syndrome, is quite rare, and has only been sparingly described. While cross-reactivity between antibiotics and NMBA's has been described [3] there is no described cross-reactivity between midazolam and other drugs/metabolites in current literature. Our case demonstrates the importance of 1) maintaining a high index of suspicion of anaphylaxis with sudden hemodynamic changes/collapse 2) reviewing the perioperative allergenic workup including skin testing and 3) highlighting a continued need for investigating cross-reactivity with perioperative medications.

Acknowledgements

Non-author contributor: George J Powers, CRNA Teaching Associate Anesthesiology & Pain Medicine, University of Washington School of Medicine, Seattle, WA.

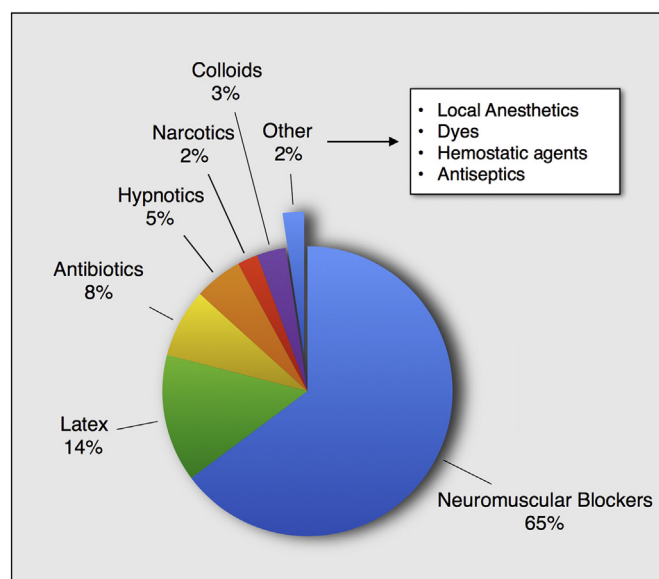


Fig. 1. Breakdown of agents responsible for IgE-mediated perioperative hypersensitivity reactions [3]. Benzodiazepines would fall into the "other" category and are considered more rare, especially in the case of midazolam.

☆ Disclosures: Leah M Landsem: none. Faith J Ross: none. Michael J Eisses: none.

☆☆ Conflicts of interest: Leah M Landsem: none. Faith J Ross: none. Michael J Eisses: none.

References

- [1] Galvão VR, Giavina-Bianchi P, Castells M. Perioperative anaphylaxis. *Curr Allergy Asthma Rep* 2014;14:452. <https://doi.org/10.1007/s11882-014-0452-6>.
- [2] Krishna MT, York M, Chin T, et al. Multi-centre retrospective analysis of anaphylaxis during general anaesthesia in the United Kingdom: aetiology and diagnostic performance of acute serum tryptase. *Clin Exp Immunol* 2014;178:399–404.
- [3] Mertes PM, Laxenaire MC. GERAP. Anaphylactic and anaphylactoid reactions occurring during anesthesia in France. Seventh epidemiologic survey (January 2001–December 2002). *Ann Fr Anesth Reanim* 2004;23(12):1133–43. <https://doi.org/10.1016/j.annfar.2004.10.013>.
- [4] Fisher MM, Baldo BA. Mast cell tryptase in anaesthetic anaphylactoid reactions. *Br J Anaesth* 1998;80(1):26–9. <https://doi.org/10.1093/bja/80.1.26>.
- [5] Mertes PM, Tajima K, Regnier-Kimmoun MA, et al. Perioperative anaphylaxis. *Med Clin N Am* 2010;94(4):761–89. <https://doi.org/10.1016/j.mcna.2010.04.002>.
- [6] Fisher MM. Clinical observations on the pathophysiology and treatment of anaphylactic cardiovascular collapse. *Anaesth Intensive Care* 1986;14:17–21.

Leah M. Landsem, MD, PGY-3¹

Anesthesiology and Pain Medicine, University of Washington School of Medicine, Seattle, WA, United States

Corresponding author at: 1959 NE Pacific St BB-1469, Seattle, WA 98195, United States.

E-mail address: live2srf@uw.edu.

Faith J. Ross, MD, Assistant Professor²

Michael J. Eisses, MD, Associate Professor²

Anesthesiology and Pain Medicine, Seattle Children's Hospital, University of Washington School of Medicine, Seattle, WA, United States

12 July 2017

Available online xxxx

¹ Primary author of manuscript, participated in editing, revision, literature review.

² Participated in editing and revising manuscript, care of the patient.