

Two Consecutive Preoperative Cardiac Arrests Involving Vancomycin in a Patient Presenting for Hip Disarticulation: A Case Report

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While an abundance of literature exists describing adverse reactions to vancomycin (eg, nausea, vomiting, red man syndrome, acute kidney injury), there is scarce evidence demonstrating vancomycin anaphylactic reactions requiring cardiopulmonary resuscitation. We report a case of a patient who had 2 separate preoperative episodes of cardiac arrest following vancomycin that occurred 4 weeks apart. Both episodes of anaphylaxis required cardiopulmonary resuscitation, which led to a successful patient outcome. We discuss identification and treatment of vancomycin-induced anaphylaxis. (A&A Case Reports. 2017;XXX:00–00.)

Informed written consent has been obtained from the patient. Vancomycin is an effective antibiotic used in oncology patients due to the high prevalence of Gram-positive bacterial infections in this patient population. A significant limitation of its usage involves adverse and hypersensitivity reactions. Adverse reactions include nephrotoxicity, ototoxicity, and hematologic toxicity.¹ Hypersensitivity reactions to vancomycin include immediate, type 1 immunoglobulin E (IgE)-mediated reactions and delayed, type 4 cell-mediated reactions. Adverse vancomycin reactions causing discontinuation of drug therapy have been observed in as high as 14% to 16% of cases in previous studies.²

A recent review by Minhas et al² identified 71 cases of hypersensitivity reactions to vancomycin between 1982 and 2015. Of these 71 cases, only 7 were identified as anaphylaxis. Of these 7 cases, only 2 required cardiopulmonary resuscitation. We present the case of a patient who received vancomycin on 2 separate occasions, 4 weeks apart, both of which led to cardiac arrest with successful cardiopulmonary resuscitation.

CASE DESCRIPTION

A 59-year-old, 80-kg woman presented for left hip disarticulation due to left thigh sarcoma. The medical history was significant for hypertension, hypothyroidism, and anxiety. The morning of surgery, the patient had taken 2 mg alprazolam, 100 mg metoprolol extended release, 100 µg levothyroxine, 5 mg oxycodone, and 20 mg escitalopram, all by mouth. Vital signs were blood pressure 112/74 mm Hg, heart rate 68 beats per minute, respiratory rate 18 breaths per minute, and oxygen saturation 95% on room air. Vancomycin 1 g was started at a slow intravenous infusion rate in the preoperative holding area a few minutes prior to departure to the operating room. The patient was taken to the operating room and transferred to the operating

table. Intravenous 1 mg midazolam was given after 5-lead electrocardiogram, pulse oximetry, and blood pressure monitors were placed. Within 1 minute after administration, the patient became unresponsive with nonpalpable pulses. Cardiopulmonary resuscitation was initiated due to pulseless electrical activity. The vancomycin infusion was immediately stopped, and the surgery was cancelled. The patient required intravenous 2 mg epinephrine to restore spontaneous circulation. Even after return of spontaneous circulation, the patient required a norepinephrine infusion for the next hour to maintain mean arterial pressure of at least 60 mm Hg. The differential diagnosis included cerebrovascular event, seizure, pulmonary embolism, myocardial infarction, sepsis, and anaphylaxis. After ruling out all of the above except for anaphylaxis, we concluded that the patient had an allergy to midazolam due to the timing of administration. Shortly after arrival in the intensive care unit, transthoracic echocardiogram revealed normal left ventricular function with an ejection fraction of 65% to 70%, no valvular abnormalities, and an otherwise unremarkable study. A 12-lead electrocardiogram showed sinus tachycardia with a rate of 133, premature atrial contractions, no evidence of ischemia, and some nonspecific ST/T changes anterolaterally. An acute coronary syndrome was ruled out by a cardiologist who noted that the initial troponin level was 0.02 ng/mL and it failed to rise after 8 hours.

Four weeks following the first attempted surgery, the patient presented for the second attempt at the left hip disarticulation. After the initial patient consultation in the preoperative area, it was decided that a lumbar epidural catheter for postoperative pain control would be placed. The initial vital signs were as follows: blood pressure 124/82 mm Hg, heart rate 82 beats per minute, respiratory rate 16 breaths per minute, oxygen saturation 97% on room air, and a temperature of 97.5°F. A lumbar epidural catheter was placed in the preoperative holding area at the lumbar 4–5 interspace using 0.5 mL of 1% lidocaine for local infiltration. Midazolam was avoided for sedation during the placement of the epidural. A test dose of 2.5 mL of 1.5% lidocaine with 1:200,000 epinephrine was administered through the epidural without any signs or symptoms consistent with intravascular or subarachnoid injection. The patient tolerated the procedure extremely well and rested comfortably in the stretcher for the next 5 minutes. Vancomycin was started prior to exiting

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the preoperative holding area, and within a few seconds, the patient began complaining of difficulty breathing and 1 minute later became unresponsive. The vancomycin was immediately stopped, and Advanced Cardiac Life Support protocol was initiated for pulseless electrical activity. Return of spontaneous circulation occurred following the administration of 1 mg epinephrine and 20 units of vasopressin. The patient was transferred to the intensive care unit intubated and sedated. The patient's hemodynamic status stabilized over the next 12 hours without the need for further inotropic support. A serum tryptase level was elevated at 125 µg/L (normal is <10.9 µg/L). The patient was taken directly to the operating room from the intensive care unit roughly 30 hours following the anaphylactic reaction, and the procedure was performed without complications. The patient was extubated on postoperative day 1 and discharged home in 9 days.

DISCUSSION

Perioperative anaphylactic and anaphylactoid reactions typically follow anesthetic induction and are most often associated with neuromuscular blocking agents and antibiotics.³ Often, the cutaneous manifestations of anaphylactic and anaphylactoid reactions are the recognized clues that signal underlying chemically or immune-mediated inflammation.

Anaphylaxis is classified as a type 1 immune-mediated allergic reaction that involves IgE release from mast cells. Anaphylactoid reactions are manifestations of a direct nonimmune-mediated release of mediators from mast cells and basophils. The most common anaphylactoid reaction from vancomycin is red man syndrome (RMS).⁴ RMS is commonly characterized by an erythematous, pruritic rash of the face, neck, and upper torso.⁴ Rarely, hypotension and angioedema can occur. RMS most often occurs 4 to 10 minutes after initiating the drug and commonly manifests because of rapid infusion of the medication. This reaction can be treated by slowing the medication infusion and administering a histamine-blocking agent.

Clinically, it is difficult to distinguish between anaphylactic and anaphylactoid reactions to vancomycin. Benzodiazepine allergy is considered rare, with an incidence ranging from 1:3500 to 1:20,000.⁵ However, it is more common than vancomycin-induced anaphylaxis, which has only been identified in 2 cases necessitating cardiopulmonary resuscitation.⁶

After the second cardiac arrest following only vancomycin and subcutaneous and epidural lidocaine administration, we concluded that the patient had an anaphylactic reaction to vancomycin. This was supported by an elevated tryptase level, which does not occur with anaphylactoid reactions.⁷ In addition to the exceedingly rare incidence of anaphylaxis secondary to local anesthetics, the patient received intravenous lidocaine for an endoscopy procedure weeks prior without any adverse reactions noted.

In our case, we erroneously attributed the first cardiac arrest to an anaphylactic reaction to midazolam. The logical temporal relationship between the administration of midazolam and subsequent cardiac arrest, the higher prevalence of IgE-mediated reactions, and the fact that only a scant amount of vancomycin had infused into the patient, all contributed to vancomycin's exculpation in this case. After we correctly identified vancomycin as the offending agent,

midazolam was removed from the patient's allergy list. This case demonstrates the problems that can arise from failing to designate the true offending agent in an anaphylactic reaction and underscores the vigilance required when assigning cause, regardless of how unlikely the agent may seem.

Multiple studies highlight the importance and substantial challenge of identifying the cause of intraoperative anaphylactic reactions. Meng et al⁸ retrospectively studied 31 patients who had an intraoperative anaphylactic event between 2013 and 2016 in the United Kingdom. Of 31 patients, 6 (19.4%) had unidentifiable causes, in spite of exhaustive testing and evaluation by allergists. Moreover, Meng et al discuss the importance of multidisciplinary collaboration between anesthesiologists and allergists when attempting to determine the cause.

In a recent study by Freundlich et al,⁹ systemic mastocytosis was found to be responsible for recurrent intraoperative episodes of hemodynamically significant anaphylaxis in one of the study patients. This disorder, which predisposes patients to non-IgE-mediated anaphylaxis due to abnormal mast cell proliferation, should always be considered in patients with multiple episodes of hemodynamically significant anaphylaxis.⁹

Although recurrent hemodynamically significant anaphylaxis is quite rare, it clearly presents a significant risk factor for recurrent anaphylaxis.⁹

Smith et al¹⁰ recently reported the case of a patient with previously undiagnosed hypertrophic cardiomyopathy who had an anaphylactic reaction to vancomycin while undergoing total hip reimplantation at The Mayo Clinic in Rochester, MN. The anesthesia team at Mayo Clinic performed due diligence by assessing for systemic mastocytosis including bone marrow biopsy and by collaborating with allergists to perform skin testing with all drugs given in the operating room, except for vancomycin, which was not tested because of a high incidence of false positivity.

The Australian and New Zealand College of Anaesthetists with The Australian and New Zealand Anaesthetic Allergy Group have developed guidelines for the initial treatment and ongoing management of anaphylaxis based on consensus guidelines and current literature.¹¹ Their guidelines involve the early use of epinephrine dosed in proportion to the severity of the drug reaction, intravenous fluid resuscitation, large bore intravenous access, and discontinuation of possible offending agents.

Even in the absence of cutaneous involvement, it is imperative that anaphylactic and anaphylactoid reactions are maintained as possible etiologies in the hemodynamically unstable patient's working differential diagnosis. With severe drug reactions involving hemodynamic collapse, vigilance is essential when attempting to identify the causative agent and avoid future exposure. Furthermore, multidisciplinary collaboration with allergists may be a worthwhile endeavor when the causative agent of an anaphylactic event remains unknown. ■■

DISCLOSURES

Name: Trip Evans, MD.

Contribution: This author helped write and edit the manuscript.

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