

# VANCOMYCIN INFUSION REACTION: A REVIEW AND CASE REPORT

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## ABSTRACT

**Introduction:** Although widely used as an alternative for surgical antibiotic prophylaxis in allergic patients to penicillin, the use of vancomycin can carry significant risks, such as a vancomycin infusion reaction that can be confused with an anaphylactic reaction. This case report and review of the topic are highly relevant to the daily practice of anesthesiologists. Case report: An ASA 1 15-year-old male patient undergoing laparoscopic cholecystectomy received vancomycin as antibiotic prophylaxis due to a history of penicillin allergy. During the infusion, he presented with a skin rash, hypotension, and tachycardia. After the medication was discontinued and an antihistamine was administered, the symptoms were resolved, and the surgical procedure and subsequent discharge from the post-anesthesia care unit occurred without any incidents. Discussion: Vancomycin infusion reaction is a non-IgE mediated event primarily associated with rapid drug infusion. The symptoms can mimic an anaphylactic reaction, with the main difference being that this is IgE-mediated. The reported case reinforces the importance of early recognition and management of the condition, as well the discussion about the real need to change surgical antibiotic prophylaxis in patients with a history of penicillin allergy, which can lead to unnecessary changes and compromise effective antimicrobial coverage.

**Keywords:** Vancomycin, Exanthema, Allergy and imunology, Drug hypersensitivity, Anaphylaxis.

## INTRODUCTION

Vancomycin infusion reaction is a condition that commonly occurs when this antibiotic is administered rapidly (within one hour), although cases have been reported even days after infusion. It is characterized by a variety of symptoms, sometimes resembling an anaphylactic reaction, including erythematous rash involving the face, neck, and chest, as well as angioedema. For this reason, the reaction was previously referred to as "Red Man Syndrome." Other manifestations include pruritus, weakness, chest pain, hypotension, shock,

and even risk of cardiopulmonary arrest. The crucial difference between the two conditions lies in their underlying mechanisms. In anaphylaxis, the reaction is IgE-mediated and requires prior exposure, whereas vancomycin infusion reaction is an anaphylactoid hypersensitivity reaction caused by histamine release from mast cells and basophils.<sup>1</sup>

Vancomycin infusion reaction usually occurs after parenteral administration; however, cases have also been reported following oral, topical, and even intraperitoneal administration. Its prevalence is not well established, ranging from approximately 5% to 50% among hospitalized patients requiring vancomycin infusion. Certain characteristics may predict a higher likelihood of this event, including age between 2 and 40 years, previous similar reactions, high drug doses, Caucasian ethnicity, and prolonged treatment duration.<sup>1</sup>

Although controversial, the use of antibiotics other than cefazolin for surgical prophylaxis in patients with a history of penicillin allergy is not recommended. There remains a widespread belief regarding a high rate of cross-reactivity between these antibiotics; however, this has not been supported by more recent studies.<sup>2</sup> Vancomycin is commonly administered in such cases in an attempt to maintain adequate prophylactic coverage, although this practice may increase the risk of surgical site infections caused by methicillin-sensitive *Staphylococcus aureus* and Gram-negative bacteria.<sup>3</sup>

Therefore, the present case report and literature review are considered relevant because they describe a patient with penicillin allergy who received vancomycin as an alternative agent, while also addressing antibiotic prophylaxis, a topic routinely encountered in anesthesiology practice.

## CASE REPORT

A 15-year-old male patient, weighing 55 kg, underwent cholecystectomy due to cholelithiasis. The patient had no comorbidities (ASA I) and no previous surgical procedures. He reported a history of allergy to amoxicillin, manifested by rash. Laboratory tests showed no significant abnormalities.

The patient was taken to the operating room, positioned supine, and standard multiparameter monitoring was applied, including electrocardiography, noninvasive blood pressure, and pulse oximetry. Peripheral venous access was established with a 20G catheter in the left upper limb.

Due to the history of amoxicillin allergy, the surgeon opted to administer intravenous vancomycin 1 g as antibiotic prophylaxis for the procedure. Therefore, infusion of the antibiotic was initiated together with dexamethasone 10 mg diluted in 100 mL of 0.9% saline solution.

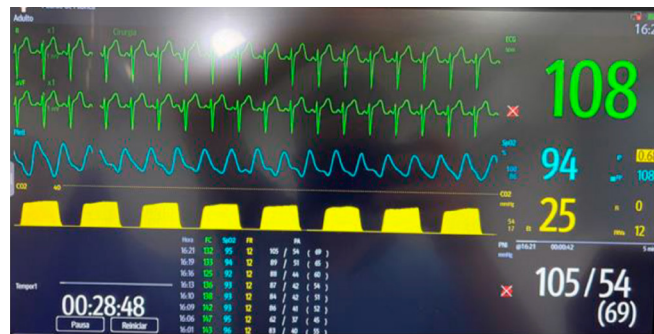
During the infusion, intravenous anesthetic induction was performed with propofol 120 mg, sufentanil 15 mcg, and cisatracurium 6 mg. Orotracheal intubation was performed under direct laryngoscopy, with a Cormack–Lehane grade I view, using an 8.0-mm cuffed endotracheal tube, with placement confirmed by capnography, without complications. Anesthesia was maintained with 2.0% sevoflurane.

Shortly after induction, the patient developed a cutaneous rash involving the face and trunk, associated with hypotension and tachycardia, as demonstrated in Figures 1 and 2. Respiratory auscultation revealed no adventitious sounds. At that moment, the vancomycin infusion was discontinued, after having been administered over approximately 20 minutes. Intravenous diphenhydramine 50 mg was then administered. Approximately 15 minutes later, vital signs had returned to normal limits, and the rash had almost completely resolved.

The surgery proceeded without further complications. The patient was extubated at the end of the procedure and transferred to the Post-Anesthesia Care Unit (PACU), being discharged after 1 hour without complications.



**Figure 1:** Example of cutaneous rash in a patient during vancomycin infusion reaction, similar to that observed in the patient described in our case report.<sup>4</sup>



**Figure 2:** Actual monitor image showing the patient's vital signs during the vancomycin infusion reaction. Persistent tachycardia and a trend toward hypotension can be observed in the preceding minutes.

## DISCUSSION

The use of antibiotics for surgical site infection prophylaxis is a fundamental measure to ensure safety in several surgical procedures. Currently, cefazolin is the antibiotic of choice according to multiple guidelines for a wide range of procedures. However, in patients with penicillin allergy associated with severe IgE-mediated reactions (bronchospasm, urticaria, documented elevated tryptase after a previous reaction, DRESS syndrome, hemolytic anemia, nephritis, anaphylaxis), replacement with non-beta-lactam antibiotics such as vancomycin or clindamycin is recommended because of the possibility of cross-reactivity between penicillins and cephalosporins. Historically, this cross-reactivity was estimated to occur in approximately 10% of cases; however, more recent studies suggest that this rate is considerably lower.<sup>2,3</sup>

Although the prevalence of penicillin allergy in the general population is estimated to range from 8% to 15%, most cases are not IgE-mediated or related to immediate

hypersensitivity reactions, instead presenting milder symptoms such as morbilliform rash, gastrointestinal symptoms, isolated pruritus, or headache. This may be explained by the high rate of antigen desensitization over time, as well as misunderstanding by patients regarding whether they truly have a penicillin allergy.<sup>2,5</sup>

According to Sexton et al., the use of alternative antibiotic prophylaxis instead of cefazolin in penicillin-allergic patients is associated with a higher risk of surgical wound infection. This increased risk may be related to differences in antimicrobial spectrum coverage, in addition to unfamiliarity with alternative dosing regimens and administration schedules.<sup>3</sup>

Discovered in 1953 and initially used for the treatment of *Staphylococcus aureus* infections resistant to penicillin, vancomycin provides coverage against Gram-positive bacteria. However, it is not the preferred treatment for methicillin-sensitive *Staphylococcus aureus* (MSSA) and does not provide Gram-negative coverage, unlike cefazolin. Therefore, it may require combination with a second antibiotic when Gram-negative pathogens are involved.<sup>3,4</sup>

Previously known as “Red Man Syndrome” since its first description in the *New England Journal of Medicine* in 1985, the condition was officially renamed “vancomycin infusion reaction” in 2021, as the former term was considered stigmatizing and potentially offensive toward Native American Indigenous peoples.<sup>4</sup>

Vancomycin infusion reaction is a non-IgE-mediated reaction characterized by histamine release from basophils and mast cells, without the need for prior antigen exposure, potentially causing erythema, pruritus, and hypotension, as observed in the patient described in our case.<sup>6</sup>

The reaction typically occurs when vancomycin is infused rapidly (1 g intravenously in less than 30 minutes), although this is not an absolute rule. Cases have been reported with daily oral vancomycin administration and even several days after drug exposure. Nevertheless, current recommendations advocate slow infusions, such as 15–20 mg/kg diluted in 250 mL administered over approximately 2 hours.<sup>6,7</sup>

Most episodes develop within 10 minutes after the start of infusion and resolve within approximately 20 minutes. Management essentially consists of supportive measures commonly used in allergic reactions, including continuous monitoring, supplemental oxygen, interruption of the infusion, administration of antihistamines, and positioning the patient in Trendelenburg position. Ideally, the initial dose should be administered and the patient observed for some time before anesthetic induction, a consideration that could have been applied in our case.<sup>1,6</sup>

Importantly, vancomycin may be slowly restarted after the episode, which generally lasts around 20 minutes, and does not necessarily need to be permanently discontinued, since this is a non-IgE-mediated reaction. This approach may avoid unnecessary changes in antibiotic therapy and consequent alterations in the antimicrobial spectrum.<sup>6</sup> Subsequent doses may be administered over a longer period, such as 2 hours, in addition to prophylactic antihistamine administration before vancomycin infusion.<sup>1,8</sup> In contrast, anaphylaxis is an IgE-mediated reaction that requires prior exposure to the antigen and presents with symptoms similar to vancomycin infusion reaction, but with more severe manifestations such as angioedema and stridor. In such cases, treatment should follow anaphylaxis protocols, including administration of epinephrine.<sup>1</sup>

Thus, we believe that our patient indeed experienced a vancomycin infusion reaction. The symptoms were self-limited and without severe consequences, differing from an

anaphylactic reaction. As a criticism of the management, we may point out the short infusion time (approximately 20 minutes), which might have prevented the reaction had the infusion been administered over a longer period. Furthermore, it is debatable whether vancomycin was truly necessary based solely on the reported history of penicillin allergy.

## CONCLUSION

Antibiotic prophylaxis is part of the anesthesiologist's daily routine, as is the need to replace drugs in patients reporting allergies to commonly used antibiotics. Therefore, this case highlights the discussion regarding whether antibiotic substitution is truly necessary, as well as the importance of recognizing and managing vancomycin infusion reaction and its main differential diagnosis, anaphylactic reaction. Failure to distinguish between these conditions may lead to inappropriate discontinuation of therapy and the use of less effective agents for surgical prophylaxis.

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