

Anaphylactoid reaction to vancomycin during general anesthesia in a child patient

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Abstract

Vancomycin is an antibiotic used primarily for staphylococcal infections. It also is recommended by the American Heart Association for the prevention of subacute bacterial endocarditis in susceptible patients who are allergic to penicillin. Anaphylactic reactions to vancomycin are rare, with only two cases reported in the literature. A case of an anaphylactic reaction to vancomycin in a child patient during general anesthesia for dental surgery is reported. The patient had a ventricular septal defect and a penicillin allergy. Vancomycin IV was administered for prophylactic coverage while the patient was under general anesthesia. Immediately after infusion of the antibiotic, signs and symptoms of anaphylaxis ensued, blood pressure dropped rapidly, and a maculopapular rash developed over the patient's body. Emergency measures were taken, and eventually the patient's vital signs returned to normal and the rash subsided. Antibiotic coverage utilizing oral erythromycin was continued after completion of treatment.

Vancomycin hydrochloride^a is a potent intravenous antibiotic that primarily is indicated for the treatment of staphylococcal infections.¹ It was introduced in 1956 following a large-scale search for an antibacterial agent with high specificity and activity against *Staphylococcus aureus* which was raging out of control at that time.² Two years later, with the introduction of the semisynthetic penicillins and the cephalosporins, vancomycin virtually was discarded in favor of these less toxic agents.³ During the last several years, however, there has been a renewed interest in and use of vancomycin due to the development of staphylococcal strains resistant to the semisynthetic penicillins and cephalosporins.²

Besides being an effective antibiotic for treating serious staphylococcal infections, vancomycin plays a useful role in dentistry. It is recommended by the American Heart Association (AHA) for preventing bacterial endocarditis in susceptible dental patients who are allergic to penicillin.⁴

Like other antibiotics, vancomycin has a variety of adverse reactions including ototoxicity, nephrotoxicity, chills, fever, phlebitis, and allergic reactions manifested by urticarial skin rashes. Severe hypersensitivity reactions such as hypotension, respiratory difficulties, and vascular collapse have been reported with vancomycin, but their occurrence is rare.⁵ Only two cases of anaphylactic reactions to vancomycin have been reported.^{6,7}

This article reports a case of an anaphylactic reaction to vancomycin in a child patient during general anesthesia for comprehensive dental care. The clinical signs, symptoms, and medical management of anaphylactic shock are described.

Clinical Report

An 11-year-old, 36 kg, white female was admitted for dental rehabilitation. Her medical history indicated that she had an autistic personality with a severe behavior disorder and a ventricular septal heart defect which required prophylactic antibiotic coverage for dental treatment. Prior to admission, intramuscular sedation (meperidine 75 mg, promethazine 37.5 mg, and chlorpromazine 37.5 mg) was administered in an unsuccessful attempt to effect restorative dentistry on an outpatient basis. Erythromycin was given orally for prophylactic coverage according to AHA recommendations. Consequently, general anesthesia was considered necessary for patient management.

The patient received diphenylhydramine 25 mg PO for preoperative sedation two hours prior to anesthesia induction. She was brought to the operating room for induction under general anesthesia. After placing ECG electrodes, a blood pressure cuff, and a precordial

^a Vancocin HCl, Eli Lilly and Co.; Indianapolis, Ind.

stethoscope, an initial induction by mask inhalation using halothane/N₂O/O₂ was accomplished. Nasotracheal intubation followed without difficulty. An intravenous infusion of 250 cc 5% dextrose in Ringer's lactated solution (D₅LR) was begun. Prior to intubation, glycopyrrolate^b 0.2 mg was given intravenously. Vancomycin (20 mg/kg) in the D₅LR was infused for antibiotic prophylaxis.

Within five minutes of the vancomycin infusion, the patient's blood pressure dropped from 100 to 70 Torr systolic. She became flushed and developed a maculopapular rash over her entire body. Her blood pressure continued to decrease to 30 Torr. An automated blood pressure cuff^c was placed on the right wrist for electronic blood pressure determinations. At this point, all anesthetic agents were discontinued and she was ventilated with 100% oxygen. Resuscitation ensued using epinephrine 0.2 mg, diphenylhydramine 25 mg, and dexamethasone 12 mg. Her blood pressure began to rise, reaching a peak of 150 Torr, then stabilizing within a few minutes at 90-100 Torr. Anesthesia was continued with halothane/N₂O/O₂, but ventricular dysrhythmias developed; lidocaine 60 mg was given and the halothane was discontinued. The anesthetic then was continued uneventfully with pancuronium bromide (a muscle relaxant), nitrous oxide, and oxygen. A foley catheter was placed to provide urinary output monitoring to check for renal failure which can follow a hypotensive episode. At this point, dental treatment began.

After treatment, glycopyrrolate and neostigmine were given to reverse the muscle relaxant; satisfactory respiratory exchange was noted and the patient was extubated awake. She then was transferred to the recovery room where she was administered oxygen by nasal mask and vital signs were monitored. At the end of one hour, the patient was awake and responsive with stable vital signs. She was moved to intensive care for overnight

^b Robinul, A.H. Robins Co.; Richmond, Va.

^c Dinamap 845, Criticon Inc.; Tampa, Fla.

observation. Dexamethasone 6 mg and diphenylhydramine 25 mg were administered every 6 hours via IV for 24 hours, and oral erythromycin 500 mg every 6 hours for eight doses was prescribed to complete antibiotic coverage. She was discharged the following day with no sequelae or further complications.

Discussion

Administration

Administering antibiotics intravenously during general anesthesia is common. The advantages of this technique, include ease of administration, immediate high blood levels, and the absence of pain — a problem with intramuscular injections in the conscious patient.

Vancomycin is prepared primarily for intravenous use since it is not absorbed appreciably by the oral route; it also is painful when given intramuscularly.² The only indication for its oral administration is treating staphylococcal enterocolitis.⁸

Modes of Action

The modes of vancomycin action are complex. Basically, it has a bactericidal effect on multiplying organisms by inhibiting biosynthesis of the major cell wall polymer, peptidoglycan.⁵ The drug is bactericidal against staphylococci-hemolytic streptococci, viridans streptococci, pneumococci, Corynebacteria, and Clostridia.⁹ It is bacteriostatic against enterococci. There is no cross resistance between vancomycin and other antibiotics, and resistance is uncommon.⁵

Indications for Use

There are several indications for vancomycin. In its early use, vancomycin was shown to treat effectively soft tissue infections, pneumonia, large abscesses, and septicemia caused by *S. aureus* and *Flavobacterium*.⁹ Its most important use is treating serious staphylococcal infections in patients who are hypersensitive to the penicillins or cephalosporins, the drugs of choice against

staphylococci.⁸ Vancomycin is reported as a successful means of treatment for subacute bacterial endocarditis (SBE) due to *S. viridans* or enterococcus when the patient is allergic to penicillins. It is not used alone, however, in treating enterococcal endocarditis but in combination with streptomycin or gentamicin since it is not bactericidal for this organism.⁵ Close monitoring of the patient is paramount in this situation because of the combined toxic effects of both drugs on the eighth cranial nerve and kidneys. Some reports also have described the successful use of single IV bolus of one gram of vancomycin at 7- to 14-day intervals for prevention and treatment of staphylococcal shunt infections in patients undergoing hemodialysis.¹⁰⁻¹²

Vancomycin is useful in neurosurgery cases to help prevent wound infections and abscess formation postoperatively.^{13,14} Recent studies have determined that vancomycin enters the cerebrospinal fluid in the presence of severe meningeal inflammation; therefore, it is recommended in the treatment of bacterial meningitis caused by *S. aureus* and *Flavobacterium*.^{14,15}

Peak blood levels of 25-40 µg/ml are found one minute after a single, one-gram dose of IV vancomycin; these levels are bactericidal for most strains of staphylococci and streptococci. The serum half-life of vancomycin is six hours in patients with normal renal functions.¹⁶

Adverse Effects

Nausea, chills, fever, urticaria, macular rashes, and phlebitis at the site of injection are adverse reactions that may result from vancomycin use.⁵ Many of these adverse reactions presumably were associated with impurities found in the early preparations of the antibiotic; through further refining, a decrease in the frequency of nausea, chills, and fevers has been noted.²

The major adverse effect of vancomycin is ototoxicity resulting from prolonged usage at high serum levels in excess of therapeutic concentrations.¹⁶ Ototoxicity usually occurs at serum levels between 80 and 100 µg/ml, but rarely is seen when serum levels are around 30 µg/ml.^{17,18}

Nephrotoxicity with albuminuria casts, mild hematuria, and azotemia may occur with vancomycin usage.⁵ Vancomycin should not be utilized in patients with impaired renal function since nearly 80% of the antibiotic is excreted by the kidneys. A delay in clearance would result in high blood levels associated with drug toxicity.

Anaphylactic reactions to vancomycin have been reported, but they are rare. No practical means exists for predicting anaphylaxis to an antibiotic except with a past history of sensitivity. If other medications are administered concomitantly with the antibiotic, they also must be considered as possible etiologies for the anaphylactic reactions.

Auxiliary Drugs

This patient had received another drug, glycopyrrolate, intravenously just prior to the anaphylactic reaction. It was given to prevent bradycardia — occasionally seen with stimulation of the posterior pharyngeal wall — as well as to aid in drying secretions. Glycopyrrolate had been used previously in this patient and also was utilized at the end of the procedure with reversal of the muscle relaxant to block the cholinergic effects seen with neostigmine administration; no signs of an adverse reaction were seen with its administration. The literature contains no report of an anaphylactic reaction to glycopyrrolate. Anaphylactic reactions usually are immediate in onset as opposed to the 7- to 8-minute delay observed with the administration of the glycopyrrolate and the reactions in this patient.

Allergies

Individuals with a personal or family history of allergies (hay fever, asthma, eczema) or a previous allergy to another antibiotic are more prone to anaphylactic reactions. They should be treated cautiously, with medical personnel being prepared for an allergic reaction.¹⁸ Skin testing can aid in determining an individual's sensitivity to medications. Although skin testing may be a good preventive measure against anaphylaxis, a negative skin test does not imply complete safety. False positive results have been noted with this test.¹⁸

Cardiovascular Hypotension

Some studies have described cardiovascular hypotension with vancomycin administration, but this result was related to a rapid infusion rate rather than to an allergic reaction. A subsequent infusion of one gram in 250 ml of crystalloid solution over an hour caused no sequelae.¹⁹

Conclusion

Vancomycin's use in dentistry is limited to prophylaxis against subacute bacterial endocarditis in patients allergic to penicillin. It also can be utilized intravenously, as described in this clinical report, for patients susceptible to SBE who are allergic to penicillin and who are being treated under general anesthesia. According to the recommendations of the AHA, erythromycin should be selected to complete the prescribed regimens after the initial dose of vancomycin.

Adverse reactions to vancomycin have been reported in the literature, yet the frequency of unwanted reactions is low and usually associated with high blood concentrations (above therapeutic levels) and rapid infusion. Patients with impaired renal function are poor candidates for vancomycin. The adverse effects of the medication can be prevented both by administering the proper dosage and by infusing the drug slowly (over at least one hour) after diluting it in 100-250 ml of crystalloid solution.

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