

Case report

NOTICE: This Material may be protected by copyright law (Title 17 US Code)

Intraoperative anaphylaxis to bacitracin during pacemaker change and laser lead extraction

John F. Freiler, MD*; Kevin E. Steel, DO†; Larry L. Hagan, MD*; Melinda M. Rathkopf, MD*; and Javier Roman-Gonzalez, MD†

Background: Bacitracin is widely used in operating rooms to soak implants, irrigate compound fractures, and apply to surgical incisions. However, bacitracin is a known sensitizer and causes not only allergic contact dermatitis but also anaphylaxis.

Objective: To describe a 72-year-old woman with anaphylaxis after irrigation and packing of an infected pacemaker pocket with a bacitracin solution.

Methods: Skin prick testing to bacitracin and latex; serum tryptase, serum histamine, serum IgE to latex, and serial cardiac enzyme measurements; blood cultures, transthoracic echocardiograms, and venograms were performed to characterize the reaction.

Results: Six hours after the anaphylactic event, the patient had an elevated serum tryptase level of 49 ng/mL (reference range, 2–10 ng/mL), which normalized the next morning. She had immediate-type skin prick test reactions to full-strength bacitracin ointment (500 U/g) and bacitracin solution (150 U/mL). Serum IgE level to latex was undetectable, and results of skin testing to latex were negative.

Conclusions: To our knowledge, this is the first case report of anaphylaxis to bacitracin during pacemaker surgery. This case illustrates that intraoperative anaphylaxis to bacitracin can be life-threatening.

Ann Allergy Asthma Immunol. 2005;95:389–393.

INTRODUCTION

The antibiotic bacitracin, discovered in June 1942, is produced by the Tracey I strain of *Bacillus subtilis*. The organism was recovered from damaged tissue and street dirt debrided from the compound fracture of a child named Tracey. The antibiotic was therefore named “bacitracin.”¹ Considered safe and effective, bacitracin is one of the most frequently used preparations for postoperative and general wound care by the medical profession and the general public.² It is widely used in operating rooms to soak implants, irrigate compound fractures, and apply to surgical incisions.² However, bacitracin is a known sensitizer and causes not only allergic contact dermatitis but also anaphylaxis.²

There have been numerous reports of allergic reactions to topical bacitracin ointment,³ but only 7 cases of intraoperative anaphylaxis due to bacitracin have been reported. We describe a patient with anaphylaxis after irrigation and packing of an infected pacemaker pocket with a bacitracin solution.

To our knowledge, this is the first case report of anaphylaxis to bacitracin during pacemaker surgery.

CASE REPORT

A 72-year-old woman presented for pacemaker generator and lead revision owing to a pacemaker pocket infection. She had a history of complete heart block, with permanent pacemaker placement 25 years earlier, and she had undergone a generator and lead revision 10 years and 1 year previously, respectively. Owing to the complexity and duration of pacemaker change and laser lead extraction with temporary pacemaker placement, it was decided that the patient should undergo generalized sedation with anesthetic support. Other medical problems included diastolic dysfunction, hypertension, hyperlipidemia, gastroesophageal reflux disease, and osteoarthritis. Previous surgical procedures also included a hysterectomy and tonsillectomy, without any anesthetic-related complications. The patient had known allergies to penicillin, which was reported to cause a generalized rash, and to tape, which was reported to cause a localized rash.

Her routine outpatient medications included daily aspirin, carvedilol, lisinopril, furosemide, simvastatin, omeprazole, and sertraline. Physical examination before surgery demonstrated a warm erythematous swelling over the pacemaker pocket. On arrival in the operating room, she received intravenous vancomycin and levofloxacin. Anesthesia was then induced with propofol, fentanyl, succinylcholine, and lidocaine. The right femoral artery was cannulated, and a tem-

* Department of Allergy/Immunology, Wilford Hall Medical Center, Lackland AFB, Texas.

† Department of Cardiology, Wilford Hall Medical Center, Lackland AFB, Texas.

The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Air Force, the Department of Defense, or the US government.

Received for publication February 15, 2005.

Accepted for publication in revised form March 15, 2005.

porary pacemaker was placed in the right ventricle. This procedure was followed by dissection down to the pacemaker pocket, removal of the generator, and extraction of the pacemaker wires using gentle traction and a laser lead extraction system. Pocket debridement was performed without difficulty, and hemostasis was achieved using electrocautery. Three hours after anesthesia induction, the pocket was irrigated with isotonic sodium chloride and a bacitracin antibiotic solution (150,000 U/L) and packed with bacitracin-soaked gauze. Within 5 minutes, the patient's blood pressure dropped to 40/20 mm Hg, peak pressures on the ventilator rapidly increased to 37 mm Hg, and she was noted to wheeze. Fluid resuscitation was begun. A transthoracic echocardiogram did not demonstrate a pericardial effusion, and a venogram did not show any extravasations of contrast. The patient did not respond to multiple doses of phenylephrine. Her drape was pulled back, and a diffuse urticarial rash was discovered on her upper chest and arms. For treatment of suspected anaphylactic shock, the patient received epinephrine, diphenhydramine, ranitidine, methylprednisolone, albuterol, and vasopressin. The antibiotic-soaked packing was removed, and, after thorough pocket irrigation with isotonic sodium chloride, the pocket was repacked with isotonic sodium chloride-soaked gauze. The patient stabilized and was transferred to the coronary care unit.

In the coronary care unit, the patient remained intubated and received a continuous epinephrine and vasopressin drip. During the next few hours, after administration of a total of 10 L of intravenous isotonic sodium chloride, the vasopressin was tapered. The urticaria resolved, airway pressures normalized, and breath sounds improved. Six hours after her event, the patient had an elevated serum tryptase level of 49 ng/mL (reference range, 2–10 ng/mL) and a normal unfractionated serum histamine level of 32.5 ng/mL (reference range, 9–141 ng/mL). The next morning the patient's tryptase level normalized to 7 ng/mL. Serum IgE level to latex was undetectable. Serial cardiac enzyme levels were normal, blood culture results remained negative, and the patient was extubated 48 hours later. She returned to the cardiac catheterization laboratory later that week for permanent placement of a new pacemaker generator and leads. She recovered well, without any permanent sequelae.

On further questioning after extubation, the patient recalled developing substantial localized swelling of her left eye after topical administration of bacitracin to an abrasion 2 years earlier. She reportedly had used bacitracin ointment on multiple occasions before that episode but refrained from further use after the incident. She did not consider this a drug allergy.

Six weeks after hospital discharge the patient underwent skin prick testing in the Allergy and Immunology Department of Wilford Hall Medical Center. She was instructed to stop taking her β -blocker, carvedilol, 48 hours before her skin prick testing appointment. The patient was tested to commercially available bacitracin ointment (500 U/g), bacitracin solution (150 U/mL), and latex. Testing to bacitracin was accomplished by placing a small amount of full-strength

Table 1. Bacitracin Skin Prick Test Results*

| | Wheal, mm | Flare, mm |
|-------------------------------|-----------|-----------|
| Bacitracin ointment, 500 U/g | 6 × 7 | 25 × 20 |
| Bacitracin solution, 150 U/mL | 8 × 5 | 31 × 27 |
| Histamine control | 5 × 6 | 25 × 23 |
| Saline control | 0 × 0 | 0 × 0 |

*A skin test result was considered positive for a wheal 3 mm greater than the control in the presence of flare.

bacitracin ointment and solution on the patient's antecubital fossa, followed by skin prick testing with a surgical needle using the prick-and-wipe method. Readings were obtained 15 minutes after placement (Table 1). The patient had a positive reaction to full-strength bacitracin ointment and bacitracin solution on skin prick testing, with good controls (Fig 1). Skin test results to latex using a noncommercial preparation were negative. There was no wheal-and-flare response in 5 of 5 healthy volunteers tested to the full-strength bacitracin ointment and bacitracin solution.

In the present patient, the rapid onset of hemodynamic shock, elevated pressures on the ventilator, evidence of bronchial hyperreactivity, the presence of urticaria, and an elevated tryptase level confirm the diagnosis of anaphylaxis. Although the serum histamine level may be elevated in anaphylaxis, it has a very short half-life. Therefore, the normal serum histamine level in this patient several hours after her event was not surprising. Given the approximately 3 hours from initial antibiotic prophylaxis and induction of anesthesia, bacitracin was suspected as the responsible agent because of the rapid onset of symptoms after exposure to this agent. The patient's history of exposure, sensitivity, and positive skin prick test reactions to bacitracin support the diagnosis of anaphylaxis to bacitracin. In this case, exposure of vessels



Figure 1. Skin prick test results. Plus sign indicates histamine control; minus sign, saline control; FS, full-strength bacitracin solution (150 U/mL); and B, bacitracin ointment (500 U/g).

during dissection and manipulation of the surgical site after irrigation and packing with bacitracin solution likely provided a portal of entry for bacitracin into the systemic circulation. It has previously been shown that high serum drug levels can develop rapidly after the irrigation of surgical wounds with bacitracin.⁴

DISCUSSION

The incidence of anaphylaxis during general surgery varies from 1:10,000 to 1:20,000 in an Australian series and 1:13,000 in a French series.⁵ Mortality ranges from 3.4% to 6%.⁵ Smaller studies published in New Zealand, the United Kingdom, and the United States show similar incidences.⁶ The most frequent causes of anaphylaxis during surgical and medical procedures are neuromuscular blocking agents, natural rubber latex, antibiotics, and induction agents.⁵ Colloids, opioids, and radiocontrast media probably account for less than 10% of all reactions.⁵

The clinical manifestations of intraoperative anaphylaxis differ from those of anaphylactic reactions not related to surgery. Intraoperative hypersensitivity reactions are generally characterized by more severe respiratory and cardiovascular manifestations, such as hypotension and cardiovascular collapse.⁷ The diagnosis may be more difficult because patients cannot express their symptoms and because cutaneous findings, which occur less often in intraoperative anaphylaxis compared with nonsurgical anaphylaxis, may be masked by surgical drapes.⁶ The use of multiple concomitantly administered drugs during the procedure can not only alter the manifestations but can also complicate therapy.⁶ Finally, obtaining and deciphering the events in the operative report often prove to be difficult.

The purported low sensitizing potential and broad-spectrum activity of bacitracin has made it one of the most frequently prescribed medications in US emergency departments and hospitals.³ In 1992, bacitracin was the seventh most frequently prescribed medication among the 34 million injury-related emergency department visits.³ Widespread use encouraged by the belief of low sensitization potential has opened the door to rapidly increasing numbers of allergic contact dermatitis reactions.³ The North American Contact Dermatitis Group periodically collects and reports current trends in sensitization rates in patients suspect of having allergic contact dermatitis. In the group's most recent results, bacitracin was identified as the ninth most common allergen in 1998 to 2000, causing 9.2% of all positive reactions.⁸ These data represent a significant increase from 1989 to 1990, when bacitracin caused 1.5% of all positive reactions.²

In addition to the cell-mediated events of allergic contact dermatitis, potentially life-threatening anaphylactic shock attributed to bacitracin has been reported. The initial report of anaphylaxis to bacitracin was by Comaish and Cunliffe in 1967.⁹ They reported an anaphylactic episode in a woman shortly after she applied bacitracin to a stasis ulcer. She developed generalized itching, sweating, dyspnea, hypotension, and subsequent collapse. Since then, there have been

multiple case reports of bacitracin anaphylaxis, most of which have occurred after topical application.³

A comprehensive review of the English language literature was performed for intraoperative anaphylaxis to bacitracin. Only 7 cases of intraoperative anaphylaxis attributed to bacitracin have been reported (Table 2). Cases of anaphylaxis have occurred after irrigation with bacitracin solution during lumbar laminectomy,¹⁰ nephrectomy,¹¹ mediastinal irrigation,¹² and knee arthroplasty.¹³ Additional cases of anaphylaxis have occurred after exposure to packing material coated or soaked in bacitracin after septorhinoplasty¹⁴ and during breast augmentation surgery.¹⁵ Anaphylaxis has even been attributed to shunt tubing that was soaked in bacitracin before insertion of a ventriculoperitoneal shunt.¹⁶ All of these reactions were severe and resulted in cardiopulmonary collapse, which required treatment with vasoactive medications. One patient required cardioversion, and another received chest compressions. There was also 1 patient who was reported to have had protracted hypotension. All of the previously described patients survived their events. Six patients had documented previous exposure to bacitracin, and 1 patient was most likely exposed to bacitracin during treatment of chronic recurrent decubiti. Four patients were noted to have had a previous adverse reaction to bacitracin, although this did not seem to be known by their current medical providers. Of patients with previous adverse events, 1 was consistent with immediate hypersensitivity, and the remaining 3 were consistent with allergic contact dermatitis. Four patients underwent subsequent evaluation with skin prick testing to bacitracin, and all of those tested were found to be positive. No complications to skin prick testing were reported.

Our patient had severe cardiopulmonary collapse and prolonged hypotension, which required treatment with multiple vasoactive medications. It was believed that the patient's β -blocker, carvedilol, contributed to the severity of her reaction. The patient's history was notable for exposure to bacitracin and a previous adverse reaction, which was consistent with a localized cutaneous reaction. The present patient's presentation and history of exposure associated with an adverse reaction are consistent with those of previously reported cases.

Although bacitracin irrigation of surgical wounds is common, intraoperative anaphylaxis associated with bacitracin is rare. However, this case and literature review illustrates that intraoperative anaphylaxis to bacitracin is frequently life-threatening. All these patients had cardiopulmonary collapse. In addition, most of these patients had a history of an adverse reaction to topical bacitracin that was unrecognized before reexposure. Health care personnel should inquire about immediate and delayed bacitracin allergy before bacitracin is prescribed, especially if it is to be used during an operative procedure. A previous history of a hypersensitivity reaction to bacitracin may indicate the potential for a severe systemic reaction. The successful management of intraoperative anaphylaxis requires prompt recognition and stabilization of the acute event, determination of the responsible drug, and sub-

Table 2. Case Reports of Preoperative Bacitracin Anaphylaxis

| Reference | Patient age, y/sex | Exposure | Reaction | Treatment | Previous exposure to bacitracin | Previous reaction to bacitracin | Skin prick testing |
|---------------|--------------------|--------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------|---------------------------------|---------------------------------|--------------------|
| 10 | 67/M | Lumbar laminectomy intraoperative irrigation | Hypotension, tachycardia, urticaria | Epinephrine, pressors, diphenhydramine, fluid resuscitation, defibrillation | Yes | No | None |
| 11 | 36/M | Nephrectomy intraoperative irrigation | Protracted hypotension, tachycardia, erythematous rash | Pressors, diphenhydramine, methylprednisolone | Probable | No | None |
| 12 | 65/M | Mediastinal irrigation after debridement | Hypotension, flushing of face and upper extremities | Epinephrine, diphenhydramine, famotidine, fluid resuscitation | Yes | Yes, localized reaction | None |
| 13 | 62/F | Irrigation during total knee arthroplasty revision | Hypotension, tachycardia, erythematous rash | Epinephrine, pressors, diphenhydramine, ranitidine, hydrocortisone, fluid resuscitation | Yes | No | Positive* |
| 14 | 48/M | Nasal packing after septorhinoplasty | Hypotension, bradycardia, first-degree AV block, erythematous rash, facial edema, elevated airway pressures | Epinephrine, albuterol, diphenhydramine, ranitidine, hydrocortisone, fluid resuscitation, chest compression | Yes | Yes, localized reaction | Positive† |
| 15 | 21/F | Packing under pectoralis muscle during breast augmentation | Hypotension, difficult ventilation | Epinephrine, diphenhydramine, hydrocortisone | Yes | Yes, localized reaction | Positive‡ |
| 16 | 9/M | Insertion of ventriculoperitoneal shunt soaked in bacitracin | Hypotension, wheezing, elevated airway pressures, erythematous rash | Epinephrine, diphenhydramine, hydrocortisone, fluid resuscitation | Yes | Yes, anaphylaxis | Positive§ |
| Present study | 72/F | Irrigation and packing of pacemaker pocket with bacitracin | Protracted hypotension, tachycardia, wheezing, elevated airway pressures, urticaria | Epinephrine, vasopressin, albuterol, diphenhydramine, ranitidine, methylprednisolone, fluid resuscitation, blood transfusion | Yes | Yes, localized reaction | Positive¶ |

Abbreviation: AV, atrioventricular.

*Bacitracin preparation and concentration not reported.

†Bacitracin ointment (500 U/g).

‡Bacitracin solution (1:1,000 dilution of 5,000 U/mL).

§Bacitracin ointment and polymyxin B sulfate ointment containing bacitracin.

¶Bacitracin ointment (500 U/g) and bacitracin solution (150 U/mL).

sequent avoidance. Confirmation by objective testing should be considered on a case-by-case basis, and referral to an allergist is warranted.

The widespread use of bacitracin is likely contributing to a high rate of sensitization in the population at large. Limiting the use of bacitracin in emergency departments, in postsurgical wound care, and for chronic dermatoses should be considered and has been suggested previously.³ It is noteworthy

that white petrolatum was found to be as safe and effective as bacitracin as a wound care ointment for ambulatory surgery, with an equally low infection rate and minimal risk of the induction of allergy.¹⁷ Another study¹⁸ that compared the use of petrolatum fine-mesh gauze vs topical antibiotic agents for the care of uncomplicated partial-thickness outpatient burns found no difference in infection rates. Additional studies that compare the effectiveness of white petrolatum

with that of antibacterial ointments in wound care protocols is warranted because white petrolatum may prove to be a better alternative.

ACKNOWLEDGMENTS

We thank Dr D. Hodson from the Department of Dermatology, Wilford Hall Medical Center, for his assistance with photography in this case report.

REFERENCES

1. Meleney FL, Johnson BA. Bacitracin. *Am J Med.* 1949;7:794–806.
2. Sood A, Taylor JS. Bacitracin: allergen of the year. *Am J Contact Dermat.* 2003;14:3–4.
3. Jacob SE, James WD. From road rash to top allergen in a flash: bacitracin. *Dermatol Surg.* 2004;30:521–524.
4. Ericson CD, Duke JH, Pickering LK, Qadri SM. Systemic absorption of bacitracin after peritoneal lavage. *Am J Surg.* 1979;137:65–67.
5. Thong BY, Chan-Yeow, Med M. Anaphylaxis during surgical and interventional procedures. *Ann Allergy Asthma Immunol.* 2004;92:619–628.
6. Lieberman P. Anaphylactic reactions during surgical and medical procedures. *J Allergy Clin Immunol.* 2002;110:S64–S69.
7. Ebo DG, Hagedorens MM, Bridts LS, De Clerck LS, Stevens WJ. Allergic reactions occurring during anaesthesia: diagnostic approach. *Acta Clin Belg.* 2004;59:34–43.
8. Marks JG, Belsito DV, DeLeo VA, et al. North American Contact Dermatitis Group patch test results, 1998 to 2000. *Am J Contact Dermat.* 2003;14:59–62.
9. Comaish JS, Cunliffe WJ. Absorption of drugs from varicose ulcers: a cause of anaphylaxis. *Br J Clin Pract.* 1967;21:97–98.
10. Netland PA, Baumgartner JE, Andrews BT. Intraoperative anaphylaxis after irrigation with bacitracin: case report. *Neurosurgery.* 1987;21:927–928.
11. Sprung J, Schedewie HK, Kampine JP. Intraoperative anaphylactic shock after bacitracin irrigation. *Anesth Analg.* 1990;71:430–433.
12. Blas M, Brieacher KS, Lobato EB. Bacitracin irrigation: a cause of anaphylaxis in the operating room. *Anesth Analg.* 2000;91:1027–1028.
13. Antevil JL, Muldoon MP, Battaglia M, Green R. Intraoperative anaphylactic shock associated with bacitracin irrigation during revision total knee arthroplasty. *J Bone Joint Surg Am.* 2003;85:339–342.
14. Gall R, Blakely B, Warrington R, Bell DD. Intraoperative anaphylactic shock from bacitracin nasal packing after septo-rhinoplasty. *Anesthesiology.* 1999;91:1545–1547.
15. Morales CM, Verdecchia S, Lang DM. Intraoperative anaphylaxis to bacitracin during breast augmentation surgery [abstract 436]. *J Allergy Clin Immunol.* 2002;109:S149.
16. Carver ED, Braude BM, Atkinson AR, Gold M. Anaphylaxis during insertion of a ventriculoperitoneal shunt. *Anesthesiology.* 2000;93:578–579.
17. Smack DP, Harrington AC, Dunn C, et al. Infection and allergy incidence in ambulatory surgery patients using white petrolatum vs bacitracin ointment: a randomized controlled trial. *JAMA.* 1996;276:972–1028.
18. Heinrich JJ, Brand DA, Cuono CB. The role of topical treatment as a determinant of infection in outpatient burns. *J Burn Care Rehabil.* 1988;9:253–257.

Requests for reprints should be addressed to:

John F. Freiler, USAF, MC
759th MDOS/MMIA
Department of Allergy/Immunology
Wilford Hall Medical Center
2200 Bergquist Dr
Suite 1
Lackland AFB, TX 78236
E-mail: John.Freiler@lackland.af.mil