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CASE REPORT

# Invasive *Brevundimonas vesicularis* bacteremia: Two case reports and review of the literature

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There are few reports of invasive infections caused by *Brevundimonas vesicularis*. We report two cases of *B. vesicularis* bacteremia confirmed by culture and 16S rRNA sequence analysis with highly variable sensitivity to broad-spectrum antibiotics. Initial empiric therapy with anti-pseudomonal antibiotics plus trimethoprim-sulfamethoxazole for hospital-acquired *B. vesicularis* infections should be considered.
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## Introduction

*Brevundimonas vesicularis* (previously known as *Corynebacterium vesiculare* and *Pseudomonas vesicularis*) is classified as a group IV member of the genus *Pseudomonas*.[1,2] Segers et al[2] re-classified *P. diminuta* and *P. vesicularis* into a new genus (*Brevundimonas*) in 1994. Isolated from both environmental and clinical specimens,[2,3] *B. vesicularis* is an aerobic, nonsporulating and glucose non-fermenting Gram-negative bacillus (GNB) with distinct nutritional requirements and biochemical characteristics.[4,5] The organism produces slow-growing and yellow-pigmented colonies on blood and chocolate agar.[4–7] Although some authors have observed that the organism does not grow in MacConkey's agar,[4] longer incubation might reveal macroscopically-visible growth.[6] Few reports of invasive infections caused by *B. vesicularis* exist in the literature. Herein we report on two patients with *B. vesicularis* bacteremia and review the previously reported cases.

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## Case reports

### Case 1

An 83-year-old man with type 2 diabetes, poor glycemic control for 20 years and hypertension for 2 years underwent coronary artery bypass grafting for severe stenosis. Twelve days post-operatively, he developed a high fever and chills associated with progressive leukocytosis. Two sets of blood cultures showed a GNB. Empiric parenteral administration of ceftazidime was initiated. A 16S rRNA sequence analysis was used to confirm the isolates. The bacterium was then identified as *B. vesicularis*. The organism was susceptible to cefazolin, amikacin, gentamicin, ampicillin/sulbactam, piperacillin/tazobactam, ceftazidime, ceftriaxone, imipenem, cefepime and ertapenem, and was resistant to ampicillin and ciprofloxacin. Two weeks after treatment, the blood cultures were negative and the patient was discharged home without complications.

### Case 2

A 25-year-old man had anaplastic large T-cell lymphoma for 2 years. Febrile neutropenia developed 1 day after he underwent autologous peripheral blood stem-cell transplantation. Empiric parenteral administration of cefepime plus vancomycin was used. A GNB isolated from the blood was identified as *B. vesicularis*, which was confirmed by 16S rRNA sequence analysis 5 days later. The organism was susceptible to cefazolin, amikacin, gentamicin, ampicillin/sulbactam, piperacillin/tazobactam, ceftriaxone, imipenem and ertapenem, and was resistant to ampicillin, ceftazidime, cefepime and ciprofloxacin. Removal of the Hickmann catheter was followed by intravenous ceftriaxone therapy for 10 days. The subsequent blood cultures were negative and the patient was discharged home without complications 21 days after transplantation.

### Analysis

The blood cultures of the presented cases were performed using the BacT/ALERT® Microbial Detection System (bioMèrieux SA, Marcy l'Étoile, France). For identification and susceptibility testing using standard methods, the organism from the blood culture bottle was inoculated onto MacConkey's and chocolate agar plates. The identification and susceptibility testing for the isolates in our cases via the biochemical characteristics were tested by Vitek® 2 (bioMérieux, Inc., Durham, NC, USA) ID-GNB (identification of GNB) and antimicrobial susceptibility testing (alanine tminotransferase)-GN04 cards in our laboratory using the automatic Vitek 2 system based on specific characteristics, as reported previously.[3]

## Discussion

There are few reports in the literature on invasive infections caused by *B. vesicularis*. We conducted a PubMed literature search limited to English-language publications using *Pseudomonas vesicularis*, *Brevundimonas vesicularis* and *Corynebacterium vesiculare* as search terms, and 14 cases were found. The demographic data and clinical characteristics of patients with *B. vesicularis* infections are listed in Table 1.[4–16] Infections included bacteremia (10 cases), cutaneous infections (two cases), meningitis (one case), peritonitis (one case) and septic arthritis (one case). These patients were immunocompromised because of end-stage renal disease,[10,11,14] systemic lupus erythematosus involving prolonged steroid use,[4] sickle cell anemia,[5] hematological malignancy[8] and neutropenia. The incidence of bloodstream infections of *B. vesicularis* in immunocompromised as well as immunocompetent patients is increasing (Table 1). The factors predisposing patients to this infection remain unknown. Good outcomes were noted after removal of catheters in prior cases[12,14] and in one of the present cases.

Table 2 summarizes the antibiotic susceptibility and resistance of this pathogen in the previously reported and present cases. The *in vitro* antibiotic susceptibility of *B. vesicularis* is highly variable. In previously reported cases[4,16] and the present two cases of hospital-acquired bacteremia, *B. vesicularis* was resistant to ampicillin and ciprofloxacin, and in one case to ceftazidime and cefepime. Mondell[12] described a case of hospital-acquired meningitis with susceptibility to ciprofloxacin, but not to any other anti-pseudomonal antibiotics. In isolates susceptible to aminopenicillins, anti-pseudomonal penicillins, cephalosporins, carbapenems and aminoglycosides,[5,13–15] resistance to aztreonam, ceftazidime and ciprofloxacin was higher in hospital- than community-acquired organisms (Table 2).[4,12,16] Piperacillin-tazobactam and carbapenems may be more reliable antibiotics for empiric treatment of hospital-acquired bacteremia caused by *B. vesicularis*. Although no resistance to trimethoprim/sulfamethoxazole has been reported, there is no therapeutic experience with this regimen.

Our report is limited by the lack of quantitative data. The minimum inhibitory concentration and minimum bactericidal concentration were not determined. It is difficult to choose the best antimicrobial agent for the treatment of invasive *B. vesicularis* infections without these data. Eight of the previously reported cases were successfully treated with a second- or third-generation cephalosporin with or without an aminoglycoside[4,5,7,10,11,15]; three cases were treated with a β-lactam/β-lactamase inhibitor[6,8,16] and three cases were treated with ciprofloxacin alone or combined with an aminoglycoside or a monobactam[12–14] (Table 1).

Laboratory identification of *B. vesicularis* is based on colony morphology in blood agar plate, Gram stain and biochemistry test. The 16S rRNA sequencing method is a robust alternative method for the rapid identification of pathogens, especially those that are rare or difficult to identify by conventional methods. *B. vesicularis* was rapidly confirmed with 16S rRNA sequencing method compared with the GenBank reference number, as the previous method. Lee et al reported that 30 patients had *Brevundimonas* species bacteremia confirmed using the 16S rRNA sequencing method, which was more specific than commercial methods of Phoenix and the Vitek 2 system.[17]

More experience will be necessary to establish the minimum inhibitory concentration and minimum bactericidal

**Table 1** Clinical features in past English literature reporting *Brevundimonas vesicularis* infection

| No. | Age | Sex | Underlying condition(s) | Clinical presentation[a] | Source of culture | Treatment/duration[b] | Outcome | Author, year |
|---|---|---|---|---|---|---|---|---|
| 1 | 67Y | M | hemodialysis, reused dialyzers | bacteremia/HA | blood | CTX + TOB/unknown | recovered | Vanholder R, 1990 & 1992 |
| 2 | 62Y | F | hemodialysis, reused dialyzers | bacteremia/HA | blood | CTX + TOB/unknown | recovered | Vanholder R, 1990 & 1992 |
| 3 | 54Y | F | systemic lupus erythematosus, autoimmune hepatitis, steroid therapy | bacteremia/HA | blood | CTZ + TOB/15 d; debridement; skin autograft | recovered | Planes AM, 1992 |
| 4 | 5Y | M | sickle cell anemia | pneumonia/CA | blood | CRO/1 d; CRO + GM/10 d | recovered | Oberhelman RA, 1994 |
| 5 | 60Y | M | trauma | botryomycosis/CA | soft tissue | CXM/4 mo | recovered | Calegari L, 1996 |
| 6 | 42Y | F | mitral valve replacement | bacteremia/HA | blood | PIP-TZ/14 d | recovered | Gilad J, 2000 |
| 7 | 38Y | M | no | tonsillitis/CA | blood | AM-CL/3 d | recovered | Chi CY, 2004 |
| 8 | 37Y | F | acute myeloid leukemia, pregnancy, pancytopenia | necrotizing cellulitis; bacteremia/HA | blood | PIP-TZ + CC/unknown | recovered | Niedermeier DM, 2005 |
| 9 | 24Y | M | pilocytic astrocytoma | meningitis/HA | cerebral spinal fluid | CRO/not reported; CIP + AN/15 d | recovered | Mondello P, 2006 |
| 10 | 40Y | M | abscess of molar cavity | infective endocarditis/CA | blood | CZ + GM/3 d; AM-SB + GM/5 d; CRO + GM/7 d; CIP/30 d | recovered | Yang ML, 2006 |
| 11 | 55Y | M | diabetes, continuous ambulatory peritoneal dialysis | peritonitis/CA | peritoneal fluid | CZ + CTZ/3 d; Vanco + CTZ/4 d; CIP + AZN/14 d | recovered | Choi W, 2006 |
| 12 | 15 M | F | young age | septic arthritis/CA | synovial fluid | CXM/12 d; cephalexin/ 14 d | recovered | Sofer Y, 2007 |
| 13 | 71Y | M | trauma, exposed to farm animals | cutaneous infection/CA | soft tissue | cefpodoxime/7 d; AM-CL/14 d | recovered | Panasiti V, 2008 |
| 14 | 83Y | M | coronary artery bypass grafting | bacteremia/HA | blood | CTZ/14 d | recovered | present case 1 |
| 15 | 25Y | M | anaplastic large T-cell lymphoma, neutropenia | bacteremia/HA | blood | VA + FEP/5 d; CRO/10 d | recovered | present case 2 |

[a] CA = community-acquired infection; HA = hospital-acquired infection. Hospital-acquired infections are those that originate in a hospital or hospital-like settings, if they first appear 48 hours or more after admission.

[b] AM-CL = amoxicillin/clavulanate; AM-SB = ampicillin/sulbactam; AN = amikacin; AZN = aztreonam; CC = clindamycin; CIP = ciprofloxacin; CRO = ceftriaxone; CTX = cefotaxime; CTZ = ceftazidime; CXM = cefuroxime; CZ = cefazolin; GM = gentamicin; TOB = tobramycin; PIP-TZ = piperacillin/tazobactam; Vanco = vancomycin.

**Table 2** *In vitro* drug susceptibility in reported cases of *Brevundimonas vesicularis*

| Patient number[a] | 3 | 4 | 6 | 7 | 9 | 10 | 11 | 12 | 13 | case 1 | case 2 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Year | 1992 | 1994 | 2000 | 2004 | 2006 | 2006 | 2006 | 2007 | 2008 | 2009 | 2009 |
| Antibiotics[b] | HA | CA | HA | CA | HA | CA | CA | CA | CA | HA | HA |
| Ampicillin | S | — | R | R | — | S | — | S | — | R | R |
| AM-CL | — | — | S | — | — | — | — | S | S | — | — |
| AM-SB | — | — | — | — | — | — | — | — | — | S | S |
| Piperacillin | R | S | S | — | R | S | S | — | — | — | — |
| PIP-TZ | — | — | S | S | — | — | — | — | — | S | S |
| Cefazolin | S | — | — | R | R | S | — | S | — | S | S |
| Cefuroxime | — | — | R | S | — | — | — | S | R | — | — |
| Cefoxitin | S | — | — | — | — | — | — | S | R | — | — |
| Cefotaxime | S | — | — | S | — | S | — | S | — | — | — |
| Ceftriaxone | — | S | R | S | — | S | — | S | — | S | S |
| Ceftazidime | R | S | R | R | — | S | S | S | R | S | R |
| Cefepime | — | — | — | — | — | S | S | — | S | S | R |
| Gentamicin | S | S | S | R | R | S | S | S | R | S | S |
| Tobramycin | S | — | S | R | — | — | — | S | R | — | — |
| Amikacin | S | — | S | S | R | S | — | S | R | S | S |
| Imipenem | — | — | S | S | R | — | S | — | — | S | S |
| Meropenem | — | — | — | — | R | S | — | — | — | — | — |
| Ertapenam | — | — | — | — | — | — | — | — | — | S | S |
| Aztreonam | — | — | R | R | R | S | S | — | — | — | — |
| Ciprofloxacin | — | S | R | R | S | S | S | S | S | R | R |
| TMP-SXT | S | — | S | S | S | S | S | S | — | — | — |

AM-CL = amoxicillin/clavulanate; AM-SB = ampicillin/sulbactam; CA = community-acquired infection; HA = hospital-acquired infection; PIP-TZ = piperacillin/tazobactam; R = resistant; S = susceptible; TMP-SXT = trimethoprim/sulfamethoxazole; — = not determined.

[a] There were no available results of susceptibility tests in patients 1, 2, 5 and 8, as presented in Table 1.

[b] The susceptibility tests of the isolates in the reported cases and the present cases were determined by various methods, such as disc diffusion method, automatic micro-diffusion, etc.

concentration breakpoints, predisposing factors, and the choice of antibiotic therapy for *B. vesicularis* infections. Although thought to be an opportunistic pathogen in clinical practice, *B. vesicularis* may also be the cause of hospital-acquired bacteremia. Of the 22 patients with *B. vesicularis* bacteremia reported by Lee et al, infection was predominant in males (70%) and in those with underlying malignancies (55%). All community-acquired and nosocomial strains were 100% susceptible to piperacillin/tazobactam and amikacin. The mortality rate at 14 days was 14%.[17]

Empiric therapy with one antibiotic, which is used for hospital-acquired glucose nonfermenting GNB infections, seems to be unsuitable for hospital-acquired *B. vesicularis* infections. Although good outcomes have been reported in *B. vesicularis* infections, initial empiric therapy with antipseudomonal antibiotics plus trimethoprim/sulfamethoxazole for hospital-acquired *B. vesicularis* infections might be considered before completing the susceptibility tests. The optimal therapeutic duration for *B. vesicularis* infections in various situations remains to be established.

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