Emergence of *Burkholderia cepacia* in Honolulu: A Case of Nursing Home-acquired *B. cepacia* sepsis

Charles N.C. Hua MS, MSIII and Jinichi Tokeshi MD

Abstract

Burkholderia cepacia *has rarely been reported in Honolulu. Its emergence as a nursing home-acquired pathogen with high mortality rate is concerning. This case report describes a local nursing home patient who was diagnosed with* B. cepacia *sepsis in 2012.*

Keywords

Pseudomonas, Burkholderia, cepacia, nursing home, local, infection, sepsis, elderly

Introduction

Burhkholderia cepacia, formerly called *Pseudomonas cepacia*, is a gram-negative rod originally described in 1949 by an America plant pathologist named Walter H. Burkholder, Ph.D. of Cornell University, for causing a distinct stench in decaying onion bulbs called 'sour skin' disease because of its vinegar-like odor (cepacia is Latin for "onion-like").[1] *B. cepacia* is often referred to *B. cepacia* complex as a result of many unsuccessful attempts at finding an adequate technique to identify *B. cepacia*.[2] This was later found to be due to its unusually large genome resulting in marked heterogeneity among several strains identified as "B. cepacia" in the early 1990s.[2] There are currently 17 validly named species under *B. cepacia complex*.[2]

B. cepacia has emerged as an important opportunistic human respiratory pathogen in patients with cystic fibrosis resulting in abscesses and bacteremia, called "cepacia syndrome."[3-5] Community- and hospital-acquired bacteremia is uncommon in patients without cystic fibrosis, but may potentially result in sepsis, which has significant clinical importance due to its multidrug resistance, resistance to disinfectants and antiseptics, and high mortality.[6,7] In this report, we discuss and describe a case of nursing home-acquired *B. cepacia* sepsis occurring in Honolulu in 2012.

Case Report

This is an 89-year-old Japanese man, who is a long term resident of a local nursing home, with an extensive medical history of obstructive benign prostatic hyperplasia with indwelling Foley catheter, type 2 diabetes mellitus (T2DM), coronary artery disease, methicillin resistant *Staphylococcus aureus* sepsis, aspiration pneumonia, dysphagia, and status post percutaneous endoscopic gastrostomy, who was stable until 8 days prior to admission when he developed hyperglycemia (serum glucose, 500 mg/dL) and a fever (37.9 °C). His glucose was controlled and stabilized at 300 mg/dL by increasing his glargine and regular insulin, and a urinalysis with reflex culture was ordered. On the morning of admission, he was obtunded with altered mental status and his serum glucose was immeasurable. His urine culture was positive for *Burkholderia cepacia* and he was treated with ciprofloxacin at the nursing home. However, his symptoms quickly progressed and he was finally brought to the emergency department at a nearby medical center for further evaluation.

On physical exam, the patient was hypotensive (blood pressure, 80/55 mmHg), tachycardic (heart rate, 120 beats per minute), tachypneic (respiratory rate, 33 breaths per minute), and febrile (37.9°C) with coarse crackles bilaterally. Labs revealed hyperglycemia (serum glucose, 424 mg/dL) and leukocytosis (WBC, 13.4 x 10^9/L) with bandemia. His blood pressure dropped further and he was transferred to the intensive care unit (ICU) for intravenous antibiotics and further management of his deteriorating condition.

At the ICU a central line was placed and he was started on IV vancomycin 700 mg every 8 hours and IV meropenem 2 g every 8 hours. During his hospital stay, his hemoglobin dropped from 14 g/dL to 6 g/dL, and he became profoundly hypotensive. In an effort to stabilize him hemodynamically, he was given a blood transfusion, vasopressin, norepinephrine, epinephrine, and atropine. However, despite pressors and other measures, his condition continued to deteriorate and the patient expired from septic shock two days after admission.

Discussion

B. cepacia is often found as an avirulent bacterium in most healthy people, and is commonly associated with pneumonia in patients with cystic fibrosis. However, *B. cepacia* sepsis in non-cystic fibrosis patients is emerging.[6,8-10] This is the first published case report of nursing home-acquired, non-cystic fibrosis *B. cepacia* sepsis in the State of Hawai'i.

Since the patient presented with hyperglycemia and altered mental status, inadequate T2DM management was considered during the initial assessment. Infection was also considered because of his advanced age, the acute onset of fever, and severe hyperglycemia with a previous history of well-controlled T2DM. Urinary tract infection is a common cause of delirium in the elderly, and a subsequent urine culture grew *B. cepacia*. *B. cepacia* is found in many sources and has been isolated in humans, soil, plants, and river water, as well as contaminated hospital equipment and disinfectants.[2,11-13] Common hospital sources of contamination include reagents, indwelling catheters, dialysis machines, and the hands of healthcare workers.[14] The ubiquity and resistance to many antimicrobials makes this microorganism a major potential problem.

The respiratory tract is responsible for the majority of pulmonary infections with *B. cepacia* in cystic fibrosis; however, a recent study showed non-cystic fibrosis bacteremia is most commonly due to infection from central venous catheters, followed by pulmonary infections.[6,14] Most reports of *B. cepacia*

sepsis revealed the use of a vascular or Foley catheter.[15] In this case, the patient's infection may have originated from several sources, including his urinary tract due to his chronic use of a Foley catheter, his respiratory tract as evident by coarse crackles heard bilaterally, or his gastrointestinal tract secondary to his recent gastrostomy tube placement.

In this case, the initial clinical presentation of the patient along with positive urine culture for *B. cepacia* was consistent with the diagnosis of sepsis. Common identification techniques of *B. cepacia* include commercially prepared *Burkholderia cepacia* selective agar, PCR-recA amplification, and commercial test systems such as API 20NE, Phoenix, MicroScan, VITEK and VITEK 2 (bioMérieux®).[16,17] Often after identification, management of *B. cepacia* sepsis is difficult and according to a study by Ku, et al, ICU stays occurs in 44% of *B. cepacia* bacteremia.[6] Similarly, our patient was transferred to the ICU for more appropriate management of his acute sepsis.

The 2012 *Sanford Guide* recommends sulfamethoxazole-trimethoprim, meropenem, or ciprofloxacin as the treatment of choice for *B. cepacia* infections.[18] This patient was initially treated with ciprofloxacin, however, his further decompensation required the need for IV meropenem. *In vitro* studies show that breakpoint concentrations (Minimum Inhibitory Concentration) of meropenem have bacteriostatic activity.[19] Bacteriostatic therapy was decided upon in order to avoid the unwanted effect of temporary increase in inflammation associated with bactericidal drugs.[20]

Studies show that even with treatment the overall, 28-day mortality rate for *B. cepacia* infections is 41% and overall in-hospital mortality rate is approximately 52%.[6,21] The two main independent risk factors associated with increased mortality in patients with *B. cepacia* bacteremia include inappropriate initial empirical antimicrobial therapy and elevated Sequential Organ Failure Assessment (SOFA) score, which is a system used to quantify the severity of a patient's illness based on organ dysfunction.[6,22]

Conclusions

The emergence of nursing home-acquired *B. cepacia* sepsis in non-cystic fibrosis patients presents a serious threat to our community due to its resistance to antibiotics, antiseptics, and disinfectants. Multiple medical problems present in the patients of advanced age contribute to an increased mortality. Therefore, early diagnosis and aggressive treatment of elderly patients with confirmed *B. cepacia* sepsis is critical to increase the probability of survival.

Conflict of Interest

None of the authors identify a conflict of interest.

Authors' Affiliation:
- John A. Burns School of Medicine, University of Hawai'i, Honolulu, HI

Correspondence to:
Jinichi Tokeshi MD; 405 N. Kuakini St #707, Honolulu, HI 96817;
Ph: (808) 536-3267; Email: jinichi.tokeshi@gmail.com

References

1. Burkholdera WH. Sour skin, a bacteria rot of onion bulbs. *Phytopathology*. 1950;50:115-117.
2. Vandamme P, Dawyndt P. Classification and identification of the Burkholderia cepacia complex: Past, present and future. *Syst Appl Microbiol*. 2011;34:87-95.
3. Holmes A, Govan J, Goldstein R. Agricultural use of Burkholderia (Pseudomonas) cepacia: A threat to human health? *Emerging Infectious Diseases*. 1998;4:221-227.
4. Levinson W. Part IX. Brief Summaries of Medically Important Organisms. In: Levinson W, ed. *Review of Medical Microbiology and Immunology*. 11th ed. New York: McGraw-Hill; 2010.
5. Ramphal R. Chapter 152. Infections Due to *Pseudomonas* Species and Related Organisms. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012.
6. Ku NS, Han SH, Kim CO, Baek JH, Jeong SJ, Jin SJ, Choi JY, Song YG, Kim JM. Risk factors for mortality in patients with Burkholderia cepacia complex bacteraemia. *Scand J Infect Dis* . 2011;43:792-797.
7. Mann T, Ben-David D, Zlotkin A, Shachar D, Keller N, Toren A, Nagler A, Smollan G, Barzilai A, Rahav G. An outbreak of Burkholderia cenocepacia bacteremia in immunocompromised concology patients. *Infection*. 2010;38:187-194.
8. Bayram M, Bablik M, Bakan ND, Döngel I. Community-acquired burkholderia cepacia pneumonia: a report of two immunocompetent patients. *Tuberk Toraks* 2011; 59:380-383.
9. Durham SH, Lee AE, Assanasen C. Burkholderia cepacia septicemia in a pediatric oncology patient: a pharmacotherapy challenge. *Ann Pharmacother*. 2012;46:e16.
10. Varga JJ, Losada L, Zelazny AM, Brinkac L, Harkins D, Radune D, Hostetler J, Sampaio EP, Ronning CM, Nierman WC, Greenberg DE, Holland SM, Goldberg JB. Draft Genome Sequence Determination for Cystic Fibrosis and Chronic Granulomatous Disease Burkholderia multivorans Isolates. *J Bacteriol*. 2012;194:6356-6357.
11. Hardy PC, Ederer GM, Matsen JM. Contamination of commercially packaged urinary catheter kits with the pseudomonad EO-1. *N Engl J Med*. 1970;282:33-35.
12. Palleroni NJ, Holmes B. Pseudomonas cepacia sp. nov, nom. rev. *Int. J. Syst. Bacteriol*. 1981;31:479-481.
13. Sobel JD, Hashman N, Reinherz G, Merzbach D. Nosocomial Pseudomonas cepacia infection associated with chlorhexidine contamination. *Am J Med*. 1982;73:183-186.
14. Bressler AM, Kaye KS, LiPuma JJ, Alexander BD, Moore CM, Reller LB, Woods CW. Risk factors for Burkholderia cepacia complex bacteremia among intensive care unit patients without cystic fibrosis: a case-control study. *Infect Control Hosp Epidemiol*. 2007;28:951-958.
15. Mukhtharahmed B, Peter G. Burkholderia cepacia – An unusual organism for sepsis in ICUs. *Journal of Clinical and Diagnostic Research*. 2011;5:1281-1282.
16. Peacock SJ, Chieng G, Cheng AC, Dance DA, Amornchai P, Wongsuvan G, Teerawattanasook N, Chierakul W, Day NP, Wuthiekanun V. Comparison of ashdown's medium, burkholderia cepacia medium, and burkholderia pseudomallei selective agar for clinical isolation of burkholderia pseudomallei. *J Clin Microbiol*. 2005;43:5359-5361.
17. Oderiz S, Palau MJ, Del Palacio P, Lewis MC, Bettiol MP, Martina P, Bosch A, Yantorno OM, Gatti BM. Evaluation of commercial systems VITEK 2 and API 20NE for identification of Burkholderia cepacia complex bacteria from clinical samples. *Rev Argent Microbiol*. 2011;43:168-175.
18. Gilbert DN, Moellering RC Jr, Eliopoulos GM, Chambers HF, Saag MS. *The Sanford Guide to Antimicrobial Therapy*. 42nd ed. Sperryville, VA: Antimicrobial Therapy, Inc; 2012.
19. Peeters E, Nelis HJ, Coenye T. In vitro activity of ceftazidime, ciprofloxacin, meropenem, minocycline, tobramycin and trimethoprim/sulfamethoxazole against planktonic and sessile Burkholderia cepacia complex bacteria. *J Antimicrob Chemother*. 2009;64:801-809.
20. Peng ZY, Wang HZ, Srisawat N, Wen X, Rimmelé T, Bishop J, Singbartl K, Murugan R, Kellum JA. Bactericidal antibiotics temporarily increase inflammation and worsen acute kidney injury in experimental sepsis. *Crit Care Med*. 2012.40:538-543.
21. Liao CH, Chang HT, Lai CC, Huang YT, Hsu MS, Liu CY, Yang CJ, Hsueh PR. Clinical characteristics and outcomes of patients with Burkholderia cepacia bacteremia in an intensive care unit. *Diagn Microbiol Infect Dis*. 2011;70:260-266.
22. Vincent JL, de Mendonça A, Cantraine F, Moreno R, Takala J, Suter PM, Sprung CL, Colardyn F, Blecher S. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. *Crit Care Med*. 1998;26:1793–1800.