

## Two Novel Clinical Presentations of *Burkholderia cepacia* Infection

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**We report two cases of multidrug-resistant *Burkholderia cepacia* (*B. cepacia* genomovar I) and *Burkholderia multivorans* causing multiple liver abscesses in a patient with bronchial asthma (case 1) and peritonitis in a patient with cirrhosis and hepatitis C virus disease (case 2), respectively. Both patients were treated successfully.**

### CASE REPORTS

**Case 1.** A 56-year-old man was admitted in the gastroenterology department with a high-grade fever with chills and hiccoughs for 8 days. He was a cigarette smoker and had chronic obstructive pulmonary disease (COPD) and had been using a nebulizer for asthmatic attacks constantly for the past 4 years. He was conscious, oriented, febrile, anicteric, and pale with mildly tender hepatomegaly. Ultrasonography showed multiple echodense lesions suggestive of liver abscesses. The ultrasound-guided aspiration revealed thick brownish pus containing many polymorphonuclear leukocytes (10 to 15 polymorphonuclear leukocytes per oil immersion field) and gram-negative bacilli, both intra- and extracellularly. The specimen was negative for *Entamoeba histolytica* and *Echinococcus granulosus*. Culture grew non-lactose-fermenting, mucoid, smooth colonies with a diameter of approximately 2 mm. The colonies were made up of gram-negative rods. The gram-negative rods were motile, catalase and oxidase positive, and nitrate reduction test positive. The rods oxidized glucose, lactose, mannitol, and maltose. The rods were lysine decarboxylation positive, arginine hydrolysis negative, and resistant to polymyxin B. The polymyxin B-resistant organism was identified as *Burkholderia cepacia* by the API 20NE (Bio-Mérieux, Marcy l'Etoile, France) and RapID NF Plus systems (Innovative Diagnostics). The kits have accuracy of 70 to 95%, and the RapID NF Plus system is more sensitive for *B. cepacia* than API 20NE (5). The isolate was later confirmed to be *B. cepacia* genomovar I by the reference laboratory (SRL Ranbaxy Ltd., Mumbai, India) by molecular typing, using restriction fragment length polymorphism-mediated analysis of the 16S ribosomal DNA locus and DNA amplification fingerprinting. We have performed surveillance for the probable source of infection and to determine whether it was a hospital contaminant. The betadine (10% povidone iodine) used as a skin disinfectant, needle, cotton pack, instrument tray used during the ultrasound-guided aspiration procedure, swabs from bed linen and other materials in the patient's cubicle, and skin swabs from the patient were subjected to culture and found sterile.

The sensitivity of *B. cepacia* isolated from the liver pus sample was tested by broth microdilution according to the 2001 National Committee for Clinical Laboratory Standards (NCCLS) guidelines for aerobically growing bacteria (control strains were *Pseudomonas aeruginosa* ATCC 27853 and *Escherichia coli* ATCC 35218 for  $\beta$ -lactam/ $\beta$ -lactamase inhibitor combinations) using cation-adjusted Mueller-Hinton broth (9). In vitro, the organism was sensitive only to ciprofloxacin (1  $\mu$ g/ml) and meropenem (1  $\mu$ g/ml). The patient was given meropenem (1 g every 8 h intravenously) for 2 weeks along with anti-inflammatory drugs. He became afebrile after 3 days with significant decrease in the right upper quadrant pain. A repeat ultrasonograph showed that the size of the abscess cavities had decreased. At the follow-up examination, the patient showed marked improvement, and he was cured by the end of the month.

**Case 2.** A 53-year-old man known to have hepatitis C virus and related cirrhosis with portal hypertension, esophageal varices, and ascites, was admitted to the gastroenterology department with high-grade fever and generalized abdominal pain with distention for 3 days. He had been going to a general practitioner's clinic, and the general practitioner frequently tapped ascitic fluid. The last tapping had been done about a week earlier. The symptoms developed 3 days after the last tapping. On admission, the patient was conscious, febrile, pale, and anicteric and had anasarca, hepatosplenomegaly, ascites, and generalized abdominal tenderness. His total leukocyte count was 4,200/mm<sup>3</sup> with 70% neutrophils. His ascitic fluid samples showed 500 cells/mm<sup>3</sup> and was exudative (0.9% albumin, 2.8% protein). The isolate from the ascitic fluid was confirmed as *B. cepacia* by using API 20NE test strips and the RapID NF Plus system and as *B. multivorans* by restriction fragment length polymorphism-mediated analysis of the 16S ribosomal DNA locus and DNA amplification fingerprinting from the reference laboratory (SRL Ranbaxy Ltd.). Similar surveillance (as in case 1) for the probable source of infection and to determine whether it was a hospital contaminant was done by performing the culture of the Betadine, needle, cotton pack, instrument tray used during the ascitic fluid tapping, swabs from bed linen and other materials in the patient's cubicle, skin swabs from the patient, and all were found sterile.

As tested by broth microdilution performed according to the 2001 NCCLS guidelines for aerobically growing bacteria (9), the isolate was sensitive to ciprofloxacin (1  $\mu$ g/ml), amikacin (4

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µg/ml), and meropenem (1 µg/ml). Due to abnormal renal function, amikacin was not considered, and instead meropenem (1 g every 8 h intravenously) was given for 2 weeks. The condition of the patient gradually improved.

**Discussion.** *B. cepacia* has emerged as an important cause of morbidity and mortality in hospitalized patients, particularly in intensive care units (ICUs) and cancer centers, largely because of high intrinsic antibiotic resistance (6). In hospital settings, the pathogen has been recovered from tap and distilled water, nebulizers, dialysis machines, contaminated disinfectants, solutions, and intravenous fluids, catheters, blood gas analyzers, thermometers, ventilator temperature sensors, and intra-aortic balloon pumps (3). It causes a wide variety of infections ranging from superficial to deep-seated and disseminated infections, such as pneumonia (especially in patients with cystic fibrosis [1]), meningitis (7), peritonitis (in patients undergoing peritoneal dialysis [12]), and bronchiectasis (8).

*B. cepacia* is a rare respiratory isolate in our hospital settings, although this oxidase-positive, polymyxin B- and multi-drug-resistant nonfermenter is a causative organism for pneumonia in patients with cystic fibrosis in ICUs. The patient described in case 1 is known to have chronic obstructive pulmonary disease with bronchial asthma. He has regularly been treated with bronchodilating inhalers and oral bronchodilators and occasionally with steroids for the last 30 years, which might result in immunosuppression. For the past 4 years, he had been advised to frequently use a nebulizer at home. The most intriguing challenge was to trace the organism. We speculated that the organism had reached the lower respiratory tract (LRT) from the nebulizer, which was contaminated with *B. cepacia*. The patient had an acute attack of LRT infection about a month earlier, when he was treated empirically with broad-spectrum antibiotics without any microbiological investigations. The surveillance results showed that the isolate is not a hospital contaminant, as it was not isolated from the hospital environment of the patient. A possible explanation for the liver abscesses may be the hematogenous spread of the organism from the LRT to the liver during the acute attack. Similar episodes have been reported in ICUs where large outbreaks took place from extrinsic contamination of nebulized medications such as albuterol (3, 10). In another patient (case 2), the source of infection might be the antiseptic solution used by the general practitioner during frequent ascitic fluid tapping. The surveillance showed that the materials used during tapping of ascitic fluid in the hospital were not the source of the isolate. The antiseptic solution used by the general practitioner, al-

though it could not be traced, has been suspected to be a possible source of infection. Infection through contaminated antiseptic solutions has been reported in the literature (3). Although in both cases, the sources of infection cannot be firmly concluded, the probable sources of infection (the nebulizer in case 1 and the antiseptic solution in case 2) have been hypothesized relying only on the medical history of the patients, evidence from the hospital surveillance, and previously reported cases.

These two cases demonstrate the difficulties that microbiology laboratories may face in recognizing such rare pathogens. Both patients were put on meropenem, because it demonstrates good activity against *B. cepacia*, inhibiting 85 to 99% of the strains (4, 11). Moreover, it has also been shown to be 96% efficacious for intra-abdominal abscesses (2). Accurate and prompt diagnosis and treatment with newer drugs with higher tissue-penetrating ability can only save the lives of the patients. Moreover, the possibility of rare pathogens in patients regularly using nebulizers and immunosuppressive drugs should be considered.

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