INNSPUB

International Journal of Microbiology and Mycology | IJMM |
pISSN: 2309-4796
http://www.innspub.net
Vol. 9, No. 3, p. 1-6, 2019

Open Access RESEARCH PAPER

Burkholderia cepacia: A case report in the laboratory of University Hospital of Befelatanana

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Keywords: *Burkholderia cepacia*, Kidney disease, Blood culture.

Publication date: June 22, 2019

Abstract

Burkholderia cepacia has rarely been reported in Antananarivo. We present a case of a 49-year-old male with chronic kidney disease, hemodialysis-dependent, who was admitted to the hospital because of dyspnoea, deterioration of the general state and fever. His past medical history includes chronic kidney disease, hypertension, diabetes and chronic global heart failure. *Burkholderia cepacia* was identified in blood culture. The Immuno-compromised state of the patient, the antimicrobial resistance of *Burkholderia cepacia* and the delay of positivity of blood cultures are discussed.

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Introduction

Chronic renal failure is a public health problem worldwide. In 2015, more than 353 million people or 5% of the world's population suffer from chronic renal failure (Ramilitiana *et al*., 2016). The survival and quality of life of these patients depend on the continued good functioning of dialysis access sites. Bloodstream infection is the leading cause of hospitalization and the second most common cause of death among patients receiving regular hemodialysis. Controlling infection in these patients is a challenge for healthcare staff because hemodialysis is an invasive procedure with an inherent infection risk. Furthermore, catheters are often manipulated during hemodialysis sessions, and patients receiving hemodialysis are immunodeficient. Bloodstream infection is caused by the nosocomial infections in the majority of cases (Gauna *et al*, 2013). Among the germs involved, *B. cepacia* (*B. cepacia*) is an aerobic, glucose–non-fermenting, gram-negative bacillus that mainly affects immunocompromised and hospitalized patients as well as those with chronic affection diseases (Lee *et al*, 2015). Patients with cystic fibrosis and dialysis-dependent patients are particularly vulnerable. Clinical manifestations are varied and run the gamut from asymptomatic colonization to necrotizing pneumonia and sepsis (Zuckerman and Seder, 2007). It is often resistant to multiple antibiotics and has been shown to grow in penicillin medium. It is known to contaminate intravenous fluids, bronchoscopes and urinary catheters (Long *et al*, 2012). The isolation of the etiologic agent and determination of antimicrobial susceptibility profile are important for achieving better prognoses. The emergence of multiresistant bacteria is a well-recognized problem. Therefore, surveillance studies are important for the monitoring of the emergence of these microorganisms, especially in immunocompromised patients, such as those undergoing hemodialysis (Gauna *et al*, 2013).

This study aims to demonstrate a case of B. cepacia sepsis in a dialysis-dependent patient who had endocarditis with past medical history of hypertension and diabetes.

Case Report

A 49-year-old Malagasy male came to the nephrology service with dyspnoea, deterioration of the general stat and fever. His past medical history includes chronic kidney disease, hypertension, diabetes and chronic global heart failure. He is hemodialysis-dependent. The clinical examination shows ascites and hepatomegaly. Cardiac auscultation shows a mitral murmur. Concerning the laboratory tests, the complete blood count showed severe normochromic anemia and leucocytosis; the C reactive protein level is high. Serum creatinine and blood urea are also elevated. Chest X-ray shows cardiomegaly with bronchopulmonary disease. Doppler echography shows endocarditis. Regarding the therapeutic, the patient was transfused, underwent intravenous antibiotic therapy (vancomycin and gentamycin) and other drugs to stabilize the general condition. After a few days of hospitalization, there was a clinical worsening associated with fever. Thus, a blood culture was done. On day 6, blood culture grew *B. cepacia.*

Concerning the bacteriological diagnosis in the laboratory, the growth time of the blood culture was 6 days. Gram staining revealed gram-negative rod-shaped bacilli. The reisolation of the liquid from the blood culture flask in a Uriselect agar revealed off-white, oxidase-positive colonies (Fig.1). The identification of species from the API 20 NE strip Biomérieux® has revealed a bacteriemia with *B. cepacia*. Sensitivity to antibiotics was determined by the Mueller / Hinton agar diffusion method, according to the recommendations of the "Comité de l'antibiogramme de la Société Française de Microbiologie" (CA-SFM, 2013) (Fig. 2 and 3). Table 1 shows the interpretation of the results of the antibiograms according to Figs. 2 and 3.

Table 1. Interpretation of the results of the antibiograms of *B. cepacia* strains.

Antibiotics	Sensitive or Resistant Bacteria
Ceftazidine 30µg (CAZ 10)	Resistant
Cefepime 30 µg (CEF 30)	Resistant
Imipeneme 10 µg (IPM 10)	Sensitive
Cotrimoxazole 1,25/23,75µg (SXT 25)	Sensitive
Amikacine 30µg (AK 30)	Sensitive
Gentamicine 10µg (CN 10)	Resistant
Norfloxacin 10µg (NOR 10)	Sensitive
Ciproflocacine 5µg (CIP 5)	Sensitive
Levofloxacine 5µg (LEV 5)	Sensitive
Chloramphenicol 30µg (C 30)	Sensitive

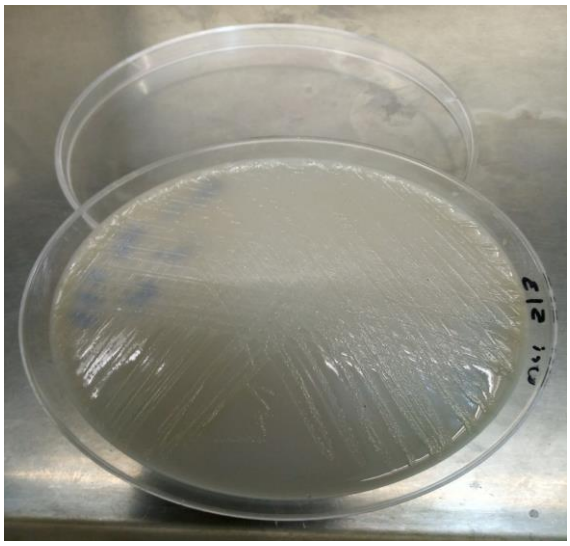

Fig. 1. Colonies of *B. cepacia.*

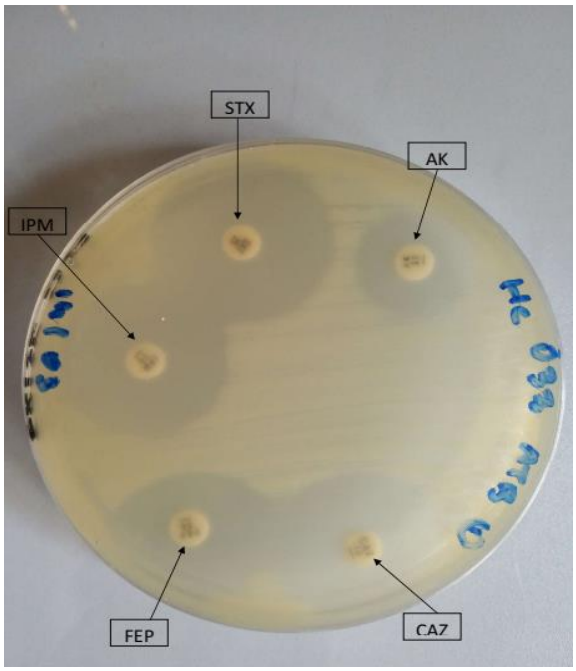

Fig. 2. Antibiogram of *B. cepacia* (petri dish n°1).

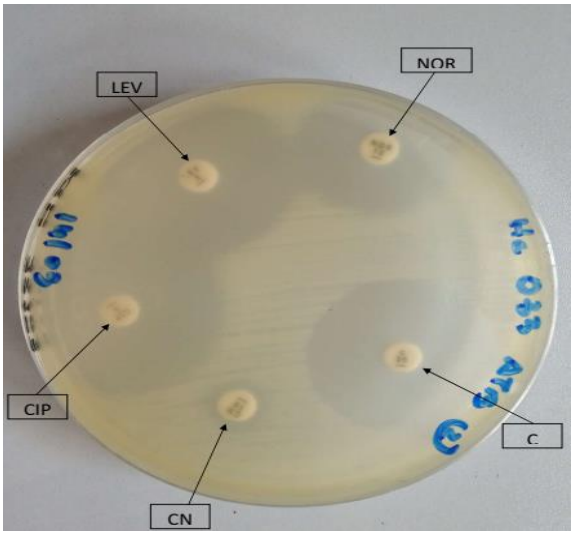

Fig. 3: Antibiogram of *B. cepacia* (petri dish n°2).

The antibiotic treatments were stopped and replaced by another antibiotic effective against *B. cepacia* (amikacin) according to the result of the antibiogram. However, the general condition of the patient deteriorated rapidly. He entered a state of septic shock leading to his death. The patient's death is due to the combination of several situations such as the patient's chronic diseases, the delay in blood culture positivity due to the slow growth of *B. cepacia* (6 days) and the inadequate probabilistic treatment (vancomycin and gentamycin).

Discussion

B. cepacia was discovered in onion roots by Walter Burkholder in 1949 at Cornell University (Bayram *et al*, 2011). *B. cepacia* refers to a group of several species of catalase-negative, non-lactose fermenting aerobic, motile, Gram-negative bacilli [4]. These organisms thrive in soil and aquatic environments (Long *et al*, 2012). *B. cepacia* has antifungal activities, and for this reason it is used as a biological control against plant-fungi (Bayram *et al*, 2011). In humans *B. cepacia* is a nosocomial organism that primarily affects patients with immune dysfunction or with preexisting damage to their respiratory epithelium. It is often resistant to multiple antibiotics and has been shown to grow in penicillin medium (Long *et al*, 2012). This

organism is not normal human flora, and is usually found in hospital environments, such as in contaminated disinfectants, nebulizer solutions, medical devices, and on the skin of healthcare workers (Alvarez-Lerma *et al*, 2008; Martin *et al*, 2012). Likewise, it is known to contaminate intravenous fluids, bronchoscopes and urinary catheters (Long *et al*, 2012). Recently, *B. cepacia* infections have increased because of increased use of broad-spectrum antimicrobial agents, longer duration of hospitalization and indwelling device-related infections (Durham *et al*, 2012). In effect, *B. cepacia* poses little risk of infection to healthy people; however it is a known important opportunistic pathogen causing morbidity and mortality due to its intrinsic resistance to most of the antibiotics in hospitalized patients (Baul *et al*, 2018).

In this study, *B. cepacia* was identified in blood culture of the patient hemodialysis-dependent. Similarly, a study by Andrea V Souza and al showed that *B. cepacia* complex was the agent most frequently recovered from blood of patients hemodialysis-dependent. According to these authors, *B. cepacia* complex was the most recurrent microorganism isolated and two of the involved patients also had *B. cepacia* complex isolated from dialysate and from arterial wound (Souza *et al*, 2004).

In effect, patients receiving long-term haemodialysis are at increased risk of bloodstream infections, usually due to repeated vascular access. Advances in aseptic techniques have reduced the risk of infection in these patients, but outbreaks continue to occur, accounting for 12–38 % of mortality in patients with chronic renal disease (Souza *et al*, 2004).

In addition to chronic renal failure, our patient also has high blood pressure, diabetes, overall heart failure and endocarditis. The combination of these infections aggravates immunodepression and promotes bacteremia. Hyun Kyun Ki and al also discovered a case of native valve endocarditis caused by *B. cepacia* (Ki *et al*, 2011).

Regarding the bacteriological diagnosis, the time of positivity of the blood culture was 6 days because *B. cepacia* is a slow-growing bacterium. The patient received probabilistic antibiotic treatment with vancomycin and gentamicin pending the outcome of the blood culture. Nevertheless, the general condition of the patient deteriorated because the probabilistic treatment was not adapted to *B. cepacia*. Indeed, the result of the antibiogram showed resistance to aminoglycosides except amikacin. So, gentamycin is not effective. Similarly, vancomycin is not effective because this glycopepetide is used instead for the treatment of Cocci infections. Indeed, the antibiotics polymyxin, gentamicin and vancomycin are used at high concentrations in *B. cepacia* selective Agar, a highly effective medium for their growth. The other bacteria present in the selective agar are sensitive to these 3 antibiotics and do not grow. This allows *B. cepacia* to grow well (Rose *et al*, 2009).

The readjustment of the treatment was no longer effective because the patient entered septic shock resulting in death. In short, the patient's death is due to the combination of several situations such as the patient's chronic diseases, the delay in blood culture positivity due to the slow growth of *B. cepacia* and the inadequate probabilistic treatment. Helen Rose and al showed that most of the patients affected by *B. cepacia* had serious underlying diseases, such as diabetes mellitus, malignancy, congestive heart failure, and chronic obstructive pulmonary disease. The mean time for a positive blood culture was 45 days after admission, 44.4% (12/27) of all deaths were directly related to *B. cepacia* bacteremia. Although *B. cepacia* infection develops in a relatively small proportion of hospitalized individuals, it has a major impact on morbidity and mortality (Rose *et al*, 2009). *Burkholderia* species are often multi-drug-resistant, and treatment is challenging. The organisms are often sensitive to trimethoprim-sulfamethoxazole, meropenem and ceftazidime (Zhou *et al*, 2007). Avegeri SG and al showed that

Sulfamethoxazole-trimethoprim has been the drug of choice for treatment. Intravenously administered antibiotic therapy, often in combination, has been successful (Avgeri *et al*, 2009).

In Madagascar, the discovery of B. cepacia is still rare. Thus, our study represents the first case of *B. cepacia* diagnosed in the Befelatanana laboratory. This study is very important for the nephrology service and the hemodialysis service which must improve their hygiene to limit the spread of this germ throughout the service.

Other germs with the same characteristics of *B. cepacia* may also be responsible for opportunistic infections. *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia* are also environmental non fermenting gram negative aerobic bacilli involved in opportunistic nosocomial infections but also in community-acquired opportunistic infections in immunocompromised patients. For these three bacteria, high-level intrinsic resistance and acquisition of antibiotic resistance mechanisms hamper therapeutic management of infections (Mérens *et al*, 2012).

Conclusion

B. cepacia is a bacterium frequently affecting hemodialysis patients because of the repetitive use of dialysate and other medical materials. Since *B. cepacia* is a slow-growing bacterium, the results of blood culture and antibiogram are often late. Thus, nephrologists should modify probabilistic treatments for killing certain suspicious germs such as *B. cepacia*. This study is very important for the nephrology service and the hemodialysis service which must improve their hygiene to limit the spread of this germ throughout the service.

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