REVIEW

Urinary tract infections with *Burkholderia cepacia*. A narrative review

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ABSTRACT

Burkholderia cepacia is an opportunistic Gram-negative bacillus that is found naturally in soil and water and usually causes respiratory infections in patients with cystic pulmonary fibrosis. Few cases of urinary tract infections with *B. cepacia* have been described in the literature, all of them clinical case presentations or case series. Therefore, we have compiled the data from the literature on this topic in a review to gain a better understanding of the etiopathogenesis, diagnosis and treatment methods of this disease. *B. cepacia* can lead to multidrug-resistant urinary tract infections in hospitals when surfaces and medical equipment are contaminated. The diagnosis is made after the onset of postoperative febrile syndrome or prolonged hospitalization in the intensive care unit. The evolution can be unfavorable, with the occurrence of sepsis and increased mortality.

KEYWORDS: *B. cepacia*; multidrug-resistant germs; urinary tract infections

INTRODUCTION

Burkholderia cepacia is the name of a complex of 17 closely related species that was known as a plant pathogen [1,2]. The *B. cepacia* complex has been used in agriculture, as an antifungal agent and in bioremediation due to its antinematode and antifungal properties as well as its ability to degrade a variety of toxic components [2-4].

In recent years, the potential of this pathogen as an opportunistic pathogen that can cause respiratory infections in patients with cystic fibrosis and chronic granulomatous disease and after lung transplantation has been demonstrated [1-3,5]. *B. cepacia* infections have been reported mainly in hospitalized patients treated with broad-spectrum antibiotics [3]. The intensive use of *B. cepacia* in agriculture has caused concern in the cystic fibrosis patient community, as well as at the level of government agencies and biomedical researchers [2]. Originally, this germ was thought to have low virulence, with a low potential to cause serious infections in humans [6], especially through contamination or colonization [7].

The presence of *B. cepacia* in liquids and aquatic settings has been reported [7]. In addition, *B. cepacia* has been detected in the aqueous hospital environment, including disinfectants and intravenous fluids, where it can persist over a long period of time [3]. It has also been detected in normal saline (0,9% sodium chloride solution) and ultrasound gel [8] and in mannitol solutions used as an irrigation medium for transurethral urologic surgery [9].

Recently, cases of urinary tract infections with *B. cepacia* have been reported [3,8,10]. Due to the rarity of these reports, there are still no studies in the literature that summarize the accumulated knowledge to date about this particular site of this infection. For this reason, we conducted a narrative review study to collect the data reported so far in the literature on the etiopathogenesis, diagnosis and treatment of this disease.

MATERIALS AND METHODS

We performed a search in the PubMed and Scopus databases using the keywords "urinary tract infections with *B. cepacia*" and "infections with *B. cepacia*". The internet search in this data basis was done for all relevant articles after 1990. 20 articles that contained urinary tract infections and *B. cepacia* in the title were found. These were all retrospective clinical case reports and case series. No prospective study, no narrative report and no systematic review were found. We then searched the above databases for the keywords *B. cepacia* infections and found 375 articles, from which we excluded the articles in languages other than English (9 articles). After reviewing the abstracts of the articles, 12 more articles related to urinary tract infections with *B. cepacia* were identified, which were included in the study. We noted all the etiopathogenic aspects, such as the

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site of contamination with the bacteria, the mode of transmission, the diagnostic and contextual stages of the infected patients, and the treatment method, depending on the sensitivity spectrum of the bacteria.

RESULTS

1. Etiopathogenesis

Urinary tract infections are in third place in terms of frequency (12%) after respiratory tract infections (68%) and blood infections (20%) [10]. Other studies have shown that the most frequent sites for *B. cepacia* infection were blood (bacteremia), skin, soft tissue, and vertebral osteomyelitis [11]. The majority are healthcare-associated infections (up to 0.7% of all nosocomial infections in a hospital) [11], mainly in intensive care units [10], and many have been reported from war zones [12]. *B. cepacia* is the most common member of the genus Burkholderia causing hospital-acquired infections. Other members of the Burkholderia complex that have been reported to cause outbreaks include *B. ambifaria, B. contaminans* and *B. stabilis* [8]. Peritonitis is another possible infection with *B. cepacia* [13,14]. *B. cepacia* keratitis following a wood chip puncture was another reported site [15].

The main source of *B. cepacia* causing urinary tract infections, but also infections in other locations, were contaminated surfaces in hospitals and person-to-person transmission [1]. The authors of other studies have identified as a source of *B. cepacia*, contaminated ultrasound gel [16], through use in transrectal prostate biopsies, with direct seeding of the prostate and bladder [17] or through use to lubricate urinary catheters that caused hospital-acquired UTIs [18]. Other studies have detected *B. cepacia* on cystoscopes [3]. In addition, *B. cepacia* has been detected in the benzalkonium chloride solution used in urinary catheter kits for self-catheterization [19], a solution used to lubricate/disinfect catheters. *B. cepacia* has also been detected in creams used in hospitals (moisturizing body milk) [20]. Contamination of disinfectants and antiseptic solutions as well as drug vials used in hospitals has also been reported [21]. Urinary tract infections occur more frequently in immunocompromised, hospitalized patients [21].

In urology departments, *B. cepacia* has been reported after bladder irrigation or the use of contaminated objects [5]. Urinary tract infections have been reported in patients who had used a contaminated 3% mannitol solution during transurethral urological procedures [9]. Neurologic bladder and vesicoureteral reflux were found to be risk factors for UTIs in *B. cepacia* [22]. Other predisposing factors were intensive care units (ICU) admission, invasive procedures including urinary catheter insertion, intravenous catheters, and intubation [6].

The evolution of urinary tract infections with *B. cepacia* carries an increased mortality risk, especially in patients with heart disease, diabetes, and bacteremia [17]. Contamination can lead to outbreaks, especially during stays in ICU, oncology wards and in patients with renal failure [3].

2. Diagnosis

No cases of community-acquired urinary tract infections have been reported to date. All cases have been reported as nosocomial hospital-acquired infections [19,23]. Urinary tract infections with *B. cepacia* have been reported in various hospital departments, most frequently in intensive care units, in patients with Foley urethral catheters [3,7,13].

In urology departments, urinary tract infections with have been reported after transurethral prostate resections, transperineal prostate biopsy, transurethral resections for bladder tumors and ureteroscopies [24]. It has also been reported in transplanted patients [22]. In most cases, the infection was objectified following the onset of postoperative febrile syndrome [22]. The recurrence of *B. cepacia* urinary infections is rare [5].

In the past, identification of the pathogen in urine culture was a difficult task for the microbiology laboratories [1] and was often misidentified, even nowadays in India [3], as *Pseudomonas* spp. *B. cepacia* was identified as non-motile, non-lactose fermentative bacteria [25], without being able to distinguish between *Pseudomonas* and *Burkholderia*.

The isolation of *B. cepacia* in blood can be performed in patients with bacteremia by incubation in 5% blood sheep agar, chocolate agar and eosin methylene blue (EBM) agar [26]. The isolates were confirmed using pulsed-field gel electrophoresis (PFGE) tests [8,19,23,26], a powerful genotyping technique used for the separation of large DNA molecules, that permits the analysis of bacterial DNA fragments [27]. Identification in urine is performed with chromogenic UTI media, followed by MALDI-TOF [13]. The minimum inhibitory concentration (MIC) of clinically relevant antibiotics was determined by standardized disc diffusion (SDD testing methods) [13]. When testing *B. cepacia*, no susceptibility method can provide reproducible and accurate MICs [13,28].

Urinary tract infections with *B. cepacia* can occur in the hospital setting at the same time as infections elsewhere [14]. Sometimes early identification of multifocal localizations can be achieved by 18F-FDG PET scan [22].

3. Clinical case

We present a particular case of a urinary tract infection with *B. cepacia* that occurred postoperatively in the form of a febrile syndrome.

A 55-year-old man with multiple right pyelocaliceal lithiasis and a negative urine culture was admitted to the urology clinic of a tertiary hospital for percutaneous nephrolithotomy. Postoperatively, about 8 hours later, he developed sepsis with fever, chills and qSOFA 3, blood count 20,000 leukocytes/mL, CRP 30mg/L and was urgently admitted to the ICU. The blood cultures performed and the urine culture, which was taken at the time of admission to the ICU, revealed multidrug-resistant *B. cepacia*, which was only sensitive to meropenem and levofloxacin. The results were reported after testing with the Microscan WalkAway DxM 1040 device (Beckman Coulter, Indianapolis, USA) and we obtained the minimum inhibitory concentration (MIC) according to the EUCAST criteria (version 14.0).

The following antibiotic discs were used: ampicillin (10 μg); amoxicillin–clavulanic acid (20–10 μg); piperacillin–tazobactam (30–6 μg); cefepime (30 μg); cefixime (5 μg); cefotaxim (5 μg); cefoxitin (30 μg); ceftazidime (10 μg); ceftazidime–avibactam (10–4 μg); cefuroxime (30 μg); ertapenem (10 μg); imipenem (10 μg); meropenem (10 μg); aztreonam (30 μg); ciprofloxacin (5 μg); levofloxacin (5 μg); ofloxacin (5 μg); amikacin (30 μg); gentamicin (10 μg); fosfomycin (200 μg; nitrofurantoin (100 μg; trimethoprim–sulfamethoxazole (1.25–23.75 μg).

The bacterium was resistant to ampicillin, ampicillin + clavulanic acid, tazobactam + piperacillin, ciprofloxacin,

ampicillin + sulbactam, ertapenem, aztreonam, fosfomycin and colistin. Under treatment with injectable levofloxacin for 10 days, the patient's condition improved with the disappearance of the inflammatory syndrome and negative urine cultures. To our knowledge, this is the first reported case of urinary tract infection with *B. cepacia* after percutaneous nephrolithotomy.

4. Treatment

B. cepacia is a multidrug-resistant pathogen, independent of the site of infection [11], with intrinsic resistance to aminoglycosides, first- and second-generation cephalosporins, antipseudomonas penicillins and polymyxins [1,29]. Resistance to tetracyclines, carbenicillin and ticarcillin has also been reported [6]. In the hospital environment, *B. cepacia* can also rapidly develop resistance to all antibiotics under the pressure of antimicrobial drugs [1]. Due to its high intrinsic resistance to antibiotics, *B. cepacia* is one of the most resistant germs encountered in the microbiology laboratory and is very difficult to treat [3]. In other studies, *B. cepacia* was found to be sensitive to ceftazidime, carbapenems and trimethoprim-sulfamethoxazole [10,12,30] and resistant to lincomycin, nalidixic acid, oxacillin, and penicillin G [25]. Other studies also reported susceptibility to levofloxacin [31].

In addition to antibiotic treatment, it was sometimes necessary to combine surgical treatment, such as graft nephrectomy, to cure the *B. cepacia* infection [32].

The mortality rate for urinary tract infections with *B. cepacia* reported in the literature was high, ranging from 11 to 31%, and was higher in cases complicated with sepsis [6,13]. Among patients with sepsis, those who presented with peritonitis and cirrhosis had a high mortality rate of 72% and multiple organ failure [14], much higher than those with urinary localization.

The best way to prevent this nosocomial infection is to take preventive measures and control the source of contamination [8,26], which is often epidemic in nature.

■ DISCUSSIONS

Data from the literature on urinary tract infections with *B. cepacia* are sparse and incomplete, with only reports of clinical cases or small series of cases. This narrative review aims to contribute to a better understanding of the etiopathogenesis, diagnosis and treatment of this rare disease. Although the urinary tract is not the most common site for *B. cepacia* infection, this etiology must be considered when dealing with a multidrug-resistant urinary tract infection. Urinary tract infections with *B. cepacia* are always transmitted by in-hospital transmission, through contaminated surfaces or contaminated medical materials and instruments, sometimes even ex-factory, from the manufacturer, such as urethral gel, mannitol solutions, etc. [8,9]. Another possible way of transmission, from person to person [1], is similar to the occurrence of urinary tract infections with other *Enteriobacteriaceae* in a urology clinic. The bacterium is always multi-resistant and, as with other hospital pathogens, occurs after endoscopic urological surgery, in patients with urinary catheters [7,33], but not after open surgery, even after complex procedures [34]. The most common urinary catheters associated with *B. cepacia* infections are urethral catheters [6], so these infections can also occur in ICU departments [21]. Diagnosis is based on urine culture, whereby modern automatic devices identify the germ without confusing it with the genus *Pseudomonas*, as was previously the case. The diagnosis is suspected after the onset of a febrile syndrome following urological procedure including kidney transplantation [22]. Treatment is mainly based on antibiotics to which the bacteria remain sensitive, such as carbapenems, levofloxacin and trimethoprim-sulfamethoxazole. Despite targeted treatment, mortality is high, but lower than in other locations of the germ.

■ CONCLUSION

B. cepacia is an opportunistic gram-negative bacillus that can cause urinary tract infections, particularly in patients after urological procedures, especially after urethral catheterization. The diagnosis is based on the detection of the germ in the urine culture after the occurrence of a post-procedural febrile syndrome. Carbapenems and quinolones are the most suitable antibiotics for treating this infection.

Disclosure

No funding sources or conflict(s) of interest to disclose.

Written informed consent

The presentation of this case was approved by the hospital's ethics committee (nr. 5414/25.06.2024). Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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