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# Ceftazidime-Resistant *Burkholderia cepacia*: An Unusual Case in a Pediatric Patient

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## ABSTRACT

Intensive care unit (ICU) sepsis in pediatric group of patients is a common clinical practice primarily in the tertiary care settings. Emergence of pathogens showing multidrug resistance pattern and causing ICU sepsis is widespread and it poses a severe threat to physicians in terms of managing their patients. At times, physicians get exposed to a pathogen they have never encountered before. *Burkholderia cepacia* infection in small children admitted in pediatric Intensive care unit (PICU) is rare. This infection is common in patients with immunocompromised immunity and underlying other debilitating disorders. We report a case of a 3 year and 06 month old female child who was diagnosed with ceftazidime-resistant *Burkholderia cepacia* in a PICU setting.

**Keywords:** Burkholderia, Ceftazidime, Drug resistant, Sepsis

## INTRODUCTION

*Burkholdria cepacia* has emerged as an important cause of hospital-acquired infections. The bacterium is known formerly as *Pseudomonas cepacia*, a gram negative aerobic, glucose, non-fermenting, motile bacillus. Immunocompromised and hospitalized patients are especially prone to this type of infection, leading to severe bacteremia that may also result in death [1]. We present a case of a 3 year and 6 month old female child who was found to have signs of respiratory tract infection followed by Burkholderia sepsis in a healthcare setting. We faced lots of difficulties in treating the patient because the pathogen was found to have resistance to ceftazidime which is usually considered as the mainstay of treatment. Informed consent was obtained from the patient's parents to report this case.

## CASE PRESENTATION

A 3 year and 6 month old female child was brought to the paediatrics emergency with high grade fever with convulsions and vomiting which was non-projectile and non-bilious. She was apparently alright five days back when she developed fever which was of sudden onset, high grade and not associated with chill and rigor. The fever was subsiding with medication and recurring again. In this current episode the fever was very high grade with convulsion and watery diarrhoea. She had developed swelling of both lower limbs and abdominal distension for 3 days which was gradual in onset.

On examination, the patient was drowsy with no signs of meningeal irritation. She was looking sick with presence of pallor and koilonychia. She had a respiratory rate of 25/min, a blood pressure of 72/54 mm Hg and a pulse of 92/min, which was regular with good volume and no radio-radial or radio-femoral delay. Systemic examination was unremarkable, including the cardiovascular, gastrointestinal, and central nervous systems. Respiratory system examination was positive for left lower lobe crepitation.

Her laboratory investigations revealed a total leukocyte count (TLC) of 26,000 cells per microliter, hemoglobin- 10 g/dL, platelets- 2,24,000/µL, creatinine- 0.5 mg/dL, blood urea- 86 mg/dL, serum albumin- 1.4 g/dL, total bilirubin- 0.2 mg/dL, serum total protein- 3.4 g/dL, serum albumin- 1.4

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g/dL, serum globulin- 2.0 g/dL, international normalized ratio (INR)- 1.6, activated partial thromboplastin time (aPTT) of 56 s and a prothrombin time (PT) of 19 s. The viral markers like HIV, HCV and HBsAg were all negative. To rule out other causes of fever like Dengue and Scrub typhus which is also seen in Odisha; samples were sent for testing by ELISA and it came to be negative.

She was put on piperacillin/tazobactam empirically. Her respiratory distress worsened over the next day; a decision was made to put her on mechanical ventilation because of acute respiratory distress syndrome (ARDS). Chest X-ray showed bilateral infiltration. Before starting the antibiotic, clinical samples like blood, urine, endotracheal tube aspirate were sent for culture sensitivity using automated BacT Alert and Vitek-2 systems. Over the coming days, her leukocytosis worsened with a TLC up to 46,000/ µL and her condition became critical with deranged renal function tests, liver functions tests, prothrombin time, and international normalized ratio (INR). Her antibiotic was changed to meropenem. The blood culture and endotracheal tube aspirate revealed the presence of ceftazidime resistant *Burkholderia cepacia* showing resistance to other antibiotics like Colistin, Imipenem, Piperacillin/Tazobactam, Ticarcillin/Clavulinic acid. As the isolated organism was sensitive to Meropenem, Cefepime, Cefoperazone/sulbactam, Ciprofloxacin, Levofloxacin and Trimethoprim/Sulfamethoxazole; the antibiotics were also changed to Meropenem. On the ninth day, the patient was weaned off from the ventilator, as the signs of sepsis were decreasing and she started with oral feeding. The antibiotic was continued and she was discharged from the hospital on the 16$^{th}$ day. She was advised to take oral Trimethoprim/Sulfamethoxazole with a regular follow-up.

## DISCUSSION

*Burkholderia cepacia* is an important nosocomial pathogen in hospitalised patients, particularly those with prior broad-spectrum antibacterial therapy. It causes infections that include bacteremia, urinary tract infection, septic arthritis, peritonitis and respiratory tract infection [2]. The respiratory tract is the most common route for an infection by *Burkholderia cepacia*, followed by intravascular catheters [3]. Our patient appeared to have an infection in the lungs accompanied by bacteremia. *Burkholderia cepacia* can also be spread directly or indirectly from saliva or fomites of patients with cystic fibrosis [4]. Risk of spread is higher by direct exchange of respiratory secretions due to kissing or intimate social contact [5]. The ability for Burkholderia species to thrive in the diverse range of environments is testament to the fact that they can be considered as one of the most versatile groups of gram-negative bacteria.

In the present case, the initial symptoms of headache, convulsions and bilateral pitting edema with abdominal distension can be explained by the septicemia. She was put on broad-spectrum antibiotics and assisted ventilation. With the help of culture and sensitivity testing, we were able to identify ceftazidime-resistant *Burkholderia cepacia*, but we were unable to identify the source of infection. We thought of bacteremia due to hospital acquired infection as the child was taking medication for the fever from several physicians on several occasions. The drug of choice for the empirical treatment of *Burkholderia cepacia* bacteremia, in this case, was meropenem as it also covered the other suspected causes of sepsis.

A similar case of an outbreak of *Burkholderia cepacia* bacteremia in a pediatric intensive care unit has been reported by Antony et al. from South India [6]. The source of this outbreak was found to be contaminated distilled water. Most of the infections caused by *Burkholderia cepacia* are found in immunocompromised patients with opportunistic infections and especially those with HIV infection and cystic fibrosis [7].

Ribonucleic acid (RNA) sequencing revealed that the overexpression of resistance nodulation-division (RND)-3 pump activity was attributed to mutations in the efflux pump regulator gene. This can account for the mechanism of ceftazidime resistance in this pathogen. In a recent study, it has been found that avibactam can restore the activity of ceftazidime in ceftazidime-resistant Burkholderia species [8].

The success of this combination of Avibactam with ceftazidime as a combination therapy is due to the ability of avibactam to inhibit class A and C β-lactamases, including class A carbapenemases (e.g. *Klebsiella pneumoniae* carbapenemase (KPC)-2). This type of combination chemotherapy may also be considered in ceftazidime resistant *Burkholderia cepacia* cases [9]. Ceftazidime-resistant *Burkholderia cepacia*; should also be considered as an important differential for the sepsis patient who initially presents with high grade fever with respiratory complaints; so that appropriate investigations can be performed in time to improve the treatment outcome.

## CONCLUSION

The emergence of Ceftazidime resistant *Burkholderia cepacia* sepsis in patients, especially in a healthcare setting, poses a significant threat to our community. More and more cases infected with *Burkholderia cepacia* are being reported from our Institution and this pathogen is becoming an increasingly common source of infection in healthcare settings. Such type of pathogenic organism is also very difficult to diagnose using conventional diagnostic methods. Availability of automated culture and sensitivity system in the hospital set up has improved the isolation and identification of such organisms. Getting the sensitivity pattern with minimum inhibitory concentration (MIC) is an added advantage for such pathogens. A high index of suspicion is required to diagnose and treat this pathogen to prevent fatal outcomes related to its disease course.

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