Burkholderia cepacia causing neonatal sepsis: a case series from a tertiary care hospital

Tiwari S,[1] Pattanaik S,[1] Kar A,[1] Beriha SS[2]

[1]Department of Microbiology, Hi-Tech Medical College & Hospital, Bhubaneswar, Odisha, India, [2]Department of Paediatrics, S.C.B. Medical College & Hospital, Cuttack, Odisha, India.

Corresponding Author: Dr Shreekant Tiwari,MD, Associate Professor, Department of Microbiology, Hi-Tech Medical College & Hospital, Bhubaneswar, Odisha, India; e-mail: drshreekant@rediffmail.com

ABSTRACT

Burkholderia cepacia is a rare cause of neonatal sepsis and is mainly transmitted through contaminated medical equipments, intravenous fluids & disinfectants. It is now increasingly recognized as an important human pathogen both in immunocompromised and hospitalized patients. It is very difficult for a microbiological laboratory to identify the non-fermenting gram-negative bacilli and there is poor laboratory proficiency in the identification of *Burkholderia cepacia*. In India most of the time, these bacteria have been ambiguously reported as non-fermenting gram negative bacilli or simply as *Pseudomonas species* as there are no precise reports on the prevalence of *Burkholderia cepacia complex* (BCC) infection. In this article we have reported six cases of *Burkholderia cepacia* causing neonatal sepsis. In our case series, patient responded very well to a combination therapy of Imipenem and Ofloxacin. In most of the cases prompt recognition and appropriate antibiotic therapy resulted in complete recovery.

Keywords: *Burkholderia cepacia*, neonatal sepsis, non-fermenters

INTRODUCTION

Burkholderia cepacia (*B.cepacia*) is an aerobic, glucose non-fermenting, motile and multidrug resistant gram negative bacilli which is not considered a part of the normal human flora. It is widely distributed in the natural environment and has been isolated from water, soil, fruits and vegetables.[1] *B. cepacia* often colonizes the lungs of patients with cystic fibrosis and has emerged as an important opportunistic pathogen in hospitalized and immunocompromised patients.[2] Prematurity, very low birth weight, exposure to invasive procedures, receiving parenteral nutrition with lipid emulsions, frequent use of broad spectrum antibiotics and indwelling catheter related infections are the most common risk factors for nosocomial sepsis in neonates.[3] Though *Burkholderia cepacia* has been widely reported as a cause of neonatal sepsis, only few cases of neonatal sepsis caused by this organism have been documented in India. In this article we have reported six cases of *B. cepacia* causing neonatal sepsis from the neonatal intensive care unit of a tertiary hospital. Out of the six neonates, five were delivered vaginally and had normal birth weight whereas one neonate was delivered prematurely by cesarean section and had low birth weight.

MATERIALS AND METHODS

Six blood samples from clinically diagnosed cases of neonatal septicemia from neonatal intensive care unit of our hospital were sent to the department of Microbiology in July 2014. Bact/Alert PF Pediatric FAN (Biomerieux, France) bottles were used for blood culture. All the blood samples showed positive within 72 hours of incubation. Then, subculture was done on 10% sheep blood agar & Mac-conkey agar and the plates were incubated aerobically at 37 ^{0}C. After 24 hours of aerobic incubation large, circular, convex and β hemolytic colonies were seen on blood agar whereas non-lactose fermenting colonies with similar morphology were seen on Mac-conkey agar. Gram's stain and oxidase tests were done from the culture plates. Gram stain showed gram negative bacilli and it was oxidase positive. Identification of the isolates up to the species level and its antibiotic sensitivity tests were done using fully automated identification system VITEK-2 (Biomerieux). Other relevant laboratory parameters of sepsis such as fever ($\geq 38^0$c), raised total white cell count, elevated C - reactive protein, reduced platelet count, raised erythrocyte sedimentation rate and raised neutrophil count were also checked in all six neonates. Environmental and epidemiological investigations were conducted to identify the source and route of infection. Environmental samples included water reservoir of incubator humidifiers, tap water, sink drains, incubator surface, respiratory devices, suction machine, suction catheters and antiseptic solutions.

RESULTS

None of the environmental samples as well as antiseptic solutions showed any growth of *B. cepacia*. Samples of intravenous solution administered to all patients were collected from stocks of each ward and from the central pharmacy (one sample from each lot). Samples were inoculated in blood culture bottle (FAN Aerobic; Biomerieux) and placed in an automated system for 7 days (Bact/Alert 3Dsystem; Biomerieux). None of the intravenous solution samples showed any growth of *B. cepacia*. Antiseptic solutions (chlorhexidine and povidone-iodine solution) were inoculated in Brain heart infusion broth and incubated at 37°c for 7 days but did not show any growth of *B. cepacia*. All the six patients had central venous catheters for parenteral nutrition. Catheter tips from all the patients were cultured by conventional method; it could be a potential source of infection. Four out of six samples showed growth and later on they were identified as *B.cepacia* by automated method (VITEK-2). Urine cultures from all the patients were negative. Five neonates responded very well to antibiotic therapy (Imipenem & Ofloxacin) that was chosen on the basis of antibiotic susceptibility testing. One neonate who was premature and in a state of shock died four days after admission. In our study identification of the isolate and its susceptibility pattern was done using fully automated identification method (VITEK-2). Imipenem was the most sensitive antibiotic followed by ofloxacin and cefoperazone-sulbactem. Patients were successfully treated using combination of imipenem & ofloxacin. Amongst more recently developed antimicrobial agents, doripenem was found to be the more effective against *BCC*.

DISCUSSION

Burkholderia cepacia complex (BCC) is an important nosocomial pathogen of humans in both immunocompromised and hospitalized patients who are infected by contact with contaminated equipment during hospitalization.[4] *BCC* bacteremia should be considered in febrile patients with nosocomial infection, especially those who have an indwelling catheter, those on ventilators, those suffering from cystic fibrosis or having immune dysfunction.[5] *BCC* causes infections that include bacteremia, urinary tract infection, septic arthritis, peritonitis and respiratory tract infection. It is recognized as an important cause of morbidity and mortality among immunocompromised and hospitalized patients because of its intrinsic resistance to antimicrobial agents.[6] *BCC* bacteremia is infrequently reported and is found mainly in immunocompromised patients. Several predisposing factors have been suggested as the major determinants for developing BCC bacteremia. These include prolonged stay in intensive care unit, major surgery, indwelling catheter etc.[7]

Even after a decade, four non-fermenting gram negative bacilli (NFGNB) continue to be recognized as notorious multidrug resistant organisms. These are *Pseudomonas aeruginosa*, *Acinetobacter calcoaceticus-baumannii complex*, *Stenotrophomonas maltophila* and *Burkholderia cepacia complex (BCC)*.[8] In India there are no precise reports on the prevalence of *Burkholderia cepacia complex* infections due to lack of awareness and difficulty in identification by routine clinical laboratories. In most of the cases, *BCC* has been ambiguously reported as non-fermenting gram-negative bacilli (NFGNB) or simply *Pseudomonas*. For this reason, reports of disease due to *BCC* are rare and have been reported from only a few tertiary care centers in north India.[9] Now *BCC* has became an increasingly common nosocomial pathogen due to its high intrinsic and acquired antimicrobial resistance, lack of effective antibiotics and its ability to survive in the environment for prolonged periods. *BCC* survives and multiplies in disinfectant solutions and intravenous fluids where it may persist for longer periods.[5]

BCC is intrinsically resistant to antimicrobial agents such as aminoglycosides, first and second generation cephalosporins, antipseudomonal penicillins and polymyxins. Some antibiotics such as carbapenem and ciprofloxacin display some in-vitro activities against this bacterium. It often develops resistant to β lactams due to presence of inducible chromosomal β lactamases and altered penicillin binding proteins.[5]On initial isolation, the organism may be susceptible to cotrimoxazole and antipseudomonal β lactams. However, under antimicrobial pressure resistance quickly develops and the clinicians frequently face such challenges. As per Clinical Laboratory Standard Institute 2013 guidelines, the drugs recommended for *Burkholderia cepacia complex* are cotrimoxazole, ceftazidime, meropenem and minocycline.[10] Chloramphenicol, levofloxacin and ticarcillin-clavulinic acid are also recommended but only after performing minimum inhibitory concentration (MIC) test because disk diffusion test is unreliable for these antibiotics.

Burkholderia cepacia complex is a dangerous pulmonary pathogen and has also been reported as a cause of bacteremia in few centers from our country. Due to its ability to survive in adverse situations *BCC* contributes to increase morbidity and mortality in hospitalized patients. *Burkholderia cepacia* bacterimia should be considered in febrile patients with nosocomial infections, especially those who have indwelling catheters, patients on ventilators or immunocompromised patients. *Burkholderia cepacia* should always be kept in mind

as a cause of septicemia in neonates to reduce mortality due to this multi drug resistant pathogen. Strict infection control procedures such as hand hygiene and avoiding unnecessary invasive procedures are the best method of preventing nosocomial infections.

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ERRATA

1. In NMCJ Vol.16, No. 2-4, December 2014 issue, Pg 109-114,the authors for the original article titled "**Occurrence of dental caries in primary and permanent dentition, oral health status and treatment needs among 12-15 year old school children of Jorpati VDC, Kathmandu**" should read as : ***Shrestha N[1],Acharya J[2], Sagtani RA[2], Shrestha R[3], Shrestha S[4]*** .The affiliation should read as: **[1]Department of Conservative Dentistry and Endodontics,Nepal Medical College and Teaching Hospital, Jorpati, Kathmandu, Nepal ,[2]Department of Community and Public Health Dentistry, Nepal Medical College and Teaching Hospital, Jorpati, Kathmandu, Nepal,[3]Department of Conservative Dentistry and Endodontics, Dhulikhel Hospital, Kathmandu University School of Medical Sciences, Dhulikhel,[4]Department of Conservative Dentistry and Endodontics, Kantipur Dental College and Hospital, Kathmandu.**The author affiliation for corresponding author should read as : **Dr. Nameeta Shrestha [1]Department of Conservative Dentistry and Endodontics, Nepal Medical College and Teaching Hospital, Jorpati, Kathmandu, Nepal**

2. In NMCJ Vol.16, No. 2-4, December 2014 issue, Pg 103-108, the sequence of authors for the original article titled **"Comparative study of glycated hemoglobin by ion exchange chromatography and affinity binding nycocard reader in type 2 diabetes mellitus"** should read as ***Gautam N[1], Jha SK[2] Dubey RK [1], Jayan A[1] ,Nepaune Y[1],Padmavathi P[1], Chaudhary S[3], Sinha AK[1].***

The Editorial Board apologizes for the errors.