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Burkholderia Cepacia Complex and Septic Transfusion Reactions: An In-depth Review

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Abstract

Burkholderia cepacia complex has become serious healthcare concern because of its association with hospital outbreaks as this microbe has remarkable capability to colonize different surfaces like catheters, IV sets, respiratory devices, nebulizers and even disinfectants. Another worrisome concern with this bacterium is the problem of antibiotic resistance which leads to increased morbidity and mortality rate of the affected individuals. As it is generally considered as a nosocomial pathogen, so the ratio of community-acquired infections is very low. Common routes of transmission of BCC are through ingestion, inhalation or subcutaneous inoculation. Affected individuals typically represents wide range of non-specific and specific symptoms and signs, which mainly depends upon the immunity level of the patient and the route of transmission. Bacteraemia caused by this organism occurs through entry of this bacterium in the blood mainly via direct venous line injection and through respiratory tract. Since there are no specific nutritional requirements as well as they have the ability to grow in damp areas, so it can colonize the ventilators and ventilation system, which eventually leads them to come into contact with epithelial barriers. These organisms ae motile because of the presence of polar flagellum and also have the ability to evade phagocytosis from macrophages and epithelial cells, hence they can easily cross the epithelial barriers and can invade the underlying tissues and cause infection there. Eventually, they infiltrate the bloodstream which results in systemic spreading of this organism throughout the body. Treatment of infections caused by Burkholderia cepacia complex is comparatively difficult as they showed remarkable resistance against various classes of antimicrobial drugs. At present, there is no commercially available vaccine against any member of the BCC complex.

Keywords: Burkhulderia Cepacia, blood transfusion.

Introduction

Burkholderia cepacia, previously referred to as Pseudomonas cepacia, has gained significant importance in recent times, particularly for individuals with compromised immune systems. This Bacterium, previously believed to be a single species, is now recognized as a complex comprising various distinct strains.

The Burkholderia cepacia complex is primarily known as a pulmonary pathogen, causing infections in individuals with conditions such as CF and chronic granulomatous disease. In rare instances, the complex has also been associated with bacteremia, often seen in patients with indwelling catheters, urinary tract infections, septic arthritis, peritonitis, and respiratory tract infections. One remarkable characteristic of this Bacterial group is its exceptional adaptability as a Gram-negative Bacterium, enabling it to thrive in a diverse range of conditions.

A moist environment is conducive to the development of Burkholderia cepacia, a highly fatal infection. Aqueous conditions, such as detergent solutions and intravenous fluids, allow Burkholderia cepacia to thrive and spread for long periods in hospitals. Dialysis patients with kidney failure have been documented with many cases of Burkholderia cepacia septicemia. Plants can also harbor these Bacteria, making them important pathogens This group of microorganisms can establish chronic and intra cellular infections in the host because of their ability to form biofilms. Hospital outbreaks specially in oncohematology are generally originate from single infected source such as various medical devices, nebulizers and other antiseptics and intravenous solutions. Environmental association of this group is not well documented yet. Among different strategies used in clinical practice, transfusion of blood also has a risk association with the spreading of infection through the possibility of transfusion-transmitted infections (TTIs).[1]

The most common infection among TTIs is sepsis which is caused by the bacterial contamination of the components of blood being transfused. The storage conditions of the blood components especially the platelets create a favourable environment for the optimal

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growth of bacterial, hence this component is more vulnerable to bacterial contamination.[2] Despite the implementation of techniques to minimize the contamination and transmission of microorganisms during blood transfusions, reports about the identification of sepsis cases caused by BCC, leads to additional challenges and focused protocols for blood safety procedures.

Epidemiology of Blood Transfusion Associated BCC Transmission

Previous studies have reported the cases of nosocomial infections caused by Pseudomonas cepacian,[3-5] water used in the serological bath to thaw the cryoprecipitates was found to be the source of contamination, and while the technique of cryoprecipitate infusions from pools was done, infections took place in vulnerable individuals who received such transfusions. Another case was reported by Dinse et al., in which a patient experienced postoperative problems after receiving autologous blood followed by vaginal hysterectomy. Blood samples were taken from the patient and culture revealed the presence of mixed growth of pseudomonas cepacia and other related organisms in patient's blood. However, source of contamination was not reported.[6] Three cases of transfusion-transmitted sepsis resulted from B. cepacia were reported in by García-Erce et al., Chlorhexidine solution that was used to clean the donor skin before phlebotomy was reported as a source of infection as upon investigation, that chlorhexidine solution was found to be contaminated with B. cepacia. García-Erce et al., highlighted the probability of bacterial contamination in antiseptics or disinfectants solutions used to clean the skin of the donor before phlebotomy. To control such transmissions of microorganism, strict quality control practices should be emphasized.[7]

Recently, cases of septic shock after the transfusion of platelet component contaminated with BCC were reported by the Sociedad de Cirugía de Bogotá-Hospital de San José in Bogotá, Colombia. Source of contamination was not well documented; however, it was thought to that it may be due to separation procedure of platelet component or any undetectable change in the storage bags.[8] De et al., reported the case of septicaemia resulted from B. cepacia in 57 years old male acute myeloid leukemic patient. Although the source of infection was not made clear, it was considered that transfusion may be the source of transmission of bacteria.[9] Ramírez-Arcos et al., reported the impact of bacterial contamination of platelet components on the platelet functions of the recipients, to whom the platelet components were transfused. Abnormality was observed in platelet function such as along with the increased expression of phosphatidylserine, 22% drop in glycoprotein IIb concentration after 72 hours of transfusion and 40% decrease in its concentration after 5 days were reported. This leads to the statement that the contaminated platelets cannot enhance the already existing platelet function ability or even cannot promote hemostatis.[10]

Various standard operating procedures for preparing and storing of blood components are followed in different countries. As an example, Japan limited the time to 85 hours for platelet storage, hence to minimize the septic events. In some countries, visual examination of the blood components is mandatory through proper protocol at every step of their production process.[11-12] In eighteen countries of Latin American, a large number of blood components, 21,808,541 were transfused in 1 years, between 2016 and 2017.[13] Six incidence cases of bacterial contamination by the Pan American Health Organization were reported, which represent the occurrence rate of 1 in 3,634,756 components. Visual examination such as volume, chemical evaluation like pH, microscopic examination such as leukocyte count and platelet count and microbiological culture techniques as well as quality control tests are only performed on 1-5% of blood components. Notably, higher rates of bacterial transmission through transfusion were observed in Oceania, North America, Africa and Europe. In contrast, Latin American hemovigilance systems, excluding Brazil, showed least number of such transfusion related infections.[14]

A study reported cases of pseudomonas contamination in blood components tainted with B, cepacia because of the use of contaminated disinfectant used to clean the skin prior to phlebotomy. Quaternary ammonium-based disinfectants, was found to be inappropriate as a disinfectant because of their compromised efficacy against some Gram-negative bacteria. Remarkably, every isolate collected from three different blood components and 1 isolate from the disinfectant represented the

similar biochemical reactions and antibiotic resistance patterns. In order to prevent transfusion related B. cepacia infection, the authors suggested to address the issue through the introduction of an alcohol-based preparation. Further investigations indicated the contamination of BCC in povidone-iodine solutions, which highlighted another significant concern.[15-17]

An analysis was carried out in 2007 by Vonberg and Gastmeier, in which they reported the association of contamination of medical devices with the nosocomial infections caused by common pathogens. Infections spread through blood products included hepatitis A virus, Serratia spp and Yersinia enterocolitica. The main pathogens lead to infections caused by various secretions and other body fluids were Burkholderia cepacia and Enterobacter spp.[17] Another study, a 63-year-old man already suffered with chronic liver and kidney disease experienced a worsened septic transfusion reaction. It was reported that patient had a transfusion platelet component which was contaminated with bacteria, prior to surgery, source of contamination was not documented, assumption was made that the infection might be spread through the damage or microleaks in the matrix bag that was used for the process of apheresis.[18] Very recently a study mentioned, even after applying disinfectants techniques, some puncture sites on blood bags are more likely to become contaminated and can transmit the infection.[19]

Why Burkholderia Cepacia Complex is a Famous Epidemic Strain

Through electron microscopy, researchers have identified five distinct forms of pili in Burkholderia cepacia complex (Burkholderia cepacia) strains. Among these forms, cable (Cbl) pili have been specifically associated with epidemic strains. Cable pili are large (2-4 nm) appendages produced in a peritrichous manner, and their primary function appears to be the aggregation of Bacterial cells into significant clumps. Studies have revealed that the intermediate filament protein cytokeratin 13 (CK13) acts as a receptor on host cells for Burkholderia cepacia strains that produce cable pili and an associated 22-kDa adhesin. Notably, Burkholderia cepacia strains that can bind to CK13 may exhibit higher contagiousness, particularly among patients with CF, due to the increased expression of CK13 in CF airway epithelial cells. It is worth mentioning that cable pili are also expressed by enterotoxigenic Escherichia coli (ETEC), belonging to the CS/CFA/I family of pili.[20] Antibiotic resistance in Gram-negative rods such as in members of Enterobacterales, non-lactose fermenters such as Pseudomonas aeruginosa and Acinetobacter baumannii, is commonly mediated by the presence of efflux pumps, which mostly include cell division (RND) systems, tripartite resistance, and nodulation.[20-22] Some multidrug-resistant bacteria, such as Burkholderia spp., exhibit amotosalen concentrations that are on par with or higher than those required for PC and plasma inactivation. Nevertheless, it has not been determined whether amotosalen successfully deactivates the BCC. Although we have tried to report the maximum number of cases associated with TTIs in this review, still many remain unreported.

Treatment Options

Among the available treatment options for Burkholderia cepacia complex (Burkholderia cepacia), ceftazidime and other extended-spectrum cephalosporins have shown the greatest effectiveness. Burkholderia cepacia exhibits inherent resistance to many other classes of antibiotics. The presence of class A beta-lactamases in Burkholderia cepacia strains contributes to their resistance against beta-lactam drugs, including ceftazidime. The PenA-PenR system, initially referred to as PenB and PenR in cepacia, was originally proposed to explain this resistance mechanism in B. cepacia. This system plays a crucial role in the activation of penB and ampC targets in the presence of antibiotics, resulting in significantly reduced susceptibilities to ceftazidime, cefotaxime, and meropenem.[22]

Preventing BCC Related TTIs

These interventions consist of three primary strategies: (i) preventing bacterial introduction during blood donation through stringent donor selection, effective skin disinfection, diversion of the initial blood volume, and meticulous monitoring of the component production process; (ii) employing diagnostic techniques, such as component culture and/or rapid detection methods, to ascertain any bacterial presence in the blood components; and (iii) applying pathogen reduction techniques. In addition, to monitor and manage effective reporting and diagnoses of transfusion-related reactions,

it is important for respective departments to empower and facilitate their staff. Studies on knowledge gaps and dissemination of results for possible nationwide replication should be undertaken by blood banks and transfusion-related institutions.

Conclusion

The cases discussed in this review highlighted the significance of implementing effective quality control procedures to minimize the level of contamination of Burkholderia cepacia complex (BCC) in blood components and to protect patients from sepsis. In storage process, temperature regulation is essential step. Various concerns have been raised recently regarding the efficacy of current techniques used for pathogen inactivation that are found to be resistant against many drugs. Maintaining hemovigilance is another important step to increase the safety of transfusions protocols. It is recommended to properly follow the guidelines of hand hygiene, limits the storage periods, regular training of the concerned staff, use effective microbial inactivation techniques, and thoroughly inspect the blood components prior to transfusion.

References

1. Saeed M, Hussain S, Rasheed F, Ahmad M, Arif M, MT HR. Silent killers: Transfusion Transmissible Infections-TTI, among asymptomatic population of Pakistan. J Pak Med Assoc. 2017;67(3):369–74.
2. Gravemann U, Handke W, Schulze TJ, Seltsam A. Growth and distribution of bacteria in contaminated whole blood and derived blood components. Transfus Med Hemother. 2024 Apr 2;51(2):75–82. https://doi.org/10.1159/000536242
3. Aneela S, Abrar S, Saeed M, Hussain S, Hannan A, Riaz S. Distribution of Extended-spectrum β-lactamase and Metallo-β-lactamase-producing Pseudomonas aeruginosa in Tertiary Care Hospitals of Lahore, Pakistan. J Islamabad Med Dent Coll. 2019 Mar 24;8(1):23–8. https://doi.org/10.35787/jimdc.v8i1.312
4. Saeed M, Rasheed F, Afzal RK, Hussain S, Riaz S, Ahmad A. Pseudomonas aeruginosa: Evaluation of pathogen burden and drug-resistance trends in a tertiary care hospital. J Coll Physicians Surg Pak. 2018 Apr;28(4):279–83. https://doi.org/10.29271/jcpsp.2018.04.279
5. Rhame FS, McCullough J, Cameron S, Streifel A, White K. Pseudomonas cepacia infections caused by thawing cryoprecipitate in a contaminated water bath. Transfusion. 1979 Nov;19:653–4.
6. Dinse H, Deusch H. Sepsis following autologous blood transfusion. Anaesthesist. 1996 May;45(5):460–3. https://doi.org/10.1007/s001010050281
7. García-Erce JA, Grasa JM, Solano VM, Gimeno JJ, López A, Hernández MJ, et al. Bacterial contamination of blood components due to Burkholderia cepacia contamination from clorhexidine bottles. Vox Sang. 2002 ;83(1):70–1. https://doi.org/10.1046/j.1423-0410.2002.00195.x
8. De Vries RR, Faber JC, editors. Hemovigilance: an effective tool for improving transfusion safety. Oxford: John Wiley & Sons; 2012. https://doi.org/10.1002/9781118338179
9. De A, Shastri JS, Malak NI, Kedia M, Sisodia H. Unusual violet coloured pigment produced by Burkholderia cepacia complex – a report of five cases from a tertiary care hospital in Mumbai. J Med Sci Health. 2022 May;8(2):173. https://doi.org/10.46347/jmsh.v8i2.21.188
10. Ramirez-Arcos S, Garcia-Otalora M, McDonald C; ISBT Transfusion-Transmitted Infectious Diseases Working Party, Subgroup on Bacteria. Microbiological environmental contamination in the blood supply chain: an international survey by the bacterial subgroup of the ISBT Transfusion-Transmitted Infectious Diseases Working Party. Vox Sang. 2023 Aug;118(8):656–65. https://doi.org/10.1111/vox.13476
11. Davies-Folorunso TO, Muhibi MA, Folorunso JB, Olaniyi OD, Ademosun AA, Abdulganiy N, et al. Bacterial contamination of blood products stored at room temperature on agitator in Lagos State, Nigeria. J Prev Diagn Treat Strateg Med. 2024 Jan 1;3(1):44–50. https://doi.org/10.4103/jpdtsm.jpdtsm_145_23
12. Pérez Aliaga AI, Labata G, Aranda A, Cardoso M, Puente F, Domingo JM, et al. Improvement of blood processing and safety by automation and pathogen reduction technology. Transfus Med Hemother. 2021 Oct 1;48(5):290–7. https://doi.org/10.1159/000516696
13. Organización Panamericana de la Salud. Suministro de sangre para transfusiones en los países de Latinoamérica y del Caribe, 2014 y 2015.
14. Otalora MA. Bacterial contamination and sepsis associated with transfusion: current status in Latin America. Ann Blood. 2021 May;1(1):1–8.
15. Ebner W, Meyer E, Schulz-Huotari C, Scholz R, Zilow G, Daschner FD. Pseudocontamination of blood components with Burkholderia cepacia during quality controls. Transfus Med. 2005 Jun;15(3):241–2. https://doi.org/10.1111/j.1365-3148.2005.00577.x
16. Panlilio AL, Beck-Sague CM, Siegel JD, Anderson RL, Yetts SY, Clark NC, et al. Infections and pseudoinfections due to povidone-iodine solution contaminated with Pseudomonas cepacia. Clin Infect Dis. 1992 May 1;14(5):1078–83. https://doi.org/10.1093/clinids/14.5.1078
17. Vonberg RP, Gastmeier P. Hospital-acquired infections related to contaminated substances. J Hosp Infect. 2007 Jan 1;65(1):15–23. https://doi.org/10.1016/j.jhin.2006.09.018
18. Fadeyi EA, Wagner SJ, Goldberg C, Lu T, Young P, Bringmann PW, et al. Fatal sepsis associated with a storage container leak permitting platelet contamination with environmental bacteria after pathogen reduction. Transfusion. 2021 Feb;61(2):641–8. https://doi.org/10.1111/trf.16210
19. Gammon RR, Reik RA, Stern M, Vassallo RR, Waxman DA, Young PP, et al. Acquired platelet storage container leaks and contamination with environmental bacteria: a preventable cause of bacterial sepsis. Transfusion. 2022 Mar;62(3):641–50. https://doi.org/10.1111/trf.16776
20. Khurshid M, Rasool MH, Ashfaq UA, Aslam B, Waseem M, Ali MA, et al. Acinetobacter baumannii sequence types harboring genes encoding aminoglycoside modifying enzymes and 16SrRNA methylase: a multicenter study from Pakistan. Infect Drug Resist. 2020 Aug 18:2855–62. https://doi.org/10.2147/IDR.S260643
21. Saeed M, Rasheed F, Hussain S, Riaz S, Hanif A, Ahmad M, et al. Acinetobacter spp: Resistance and therapeutic decisions at the turn of the novel millennium. Pak J Pharm Sci. 2018 Nov 1;31:2749–54.
22. Naz S, Rasheed F, Saeed M, Iram S, Imran AA. Bad bugs and no drugs: Activity of colistin as waging war against emerging Metallo-β-lactamases producing pathogens. Ann King Edward Med Univ. 2018 Jan 1;24(1). https://doi.org/10.21649/akemu.v24i1.2339