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Original Article

Ralstonia pickettii bloodstream infection in the patient with Guillain-Barre syndrome under plasmapheresis

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ABSTRACT

Ralstonia pickettii is a rare Gram-negative opportunistic bacterium that causes rare infections such as bacteremia, neonatal sepsis, endocarditis, and meningitis in hospitalized or immunocompromised patients. In this study, we identified and reported bloodstream infection caused by *R. pickettii* in a 15 -year-old boy patient with an autoimmune disease, Guillain-Barré syndrome, under plasmapheresis and intravenous immune globulin (IVIG) therapy. He was referred for admission to the neurology center of the teaching hospital of Shiraz, Iran for inability to walk, and lower extremity muscle weakness. After he was treated with plasmapheresis once during hospitalization, and after severe fever besides shivering blood cultures using BACT/ALERT®3D instrument were positive for *R. pickettii. According to* antibiotic susceptibility test reports, *Ciprofloxacin (*5 μg*)* was prescribed. Fortunately, after starting antibiotic treatment, blood culture results reported no growth after 5 days. Indeed, the patient was infected with nosocomial hepatitis A and URSOBIL (300 mg/BID/Po) was administered. Hence, after reporting the infection occurrence to the hospital infection control unit, initial and possible measures such as device infection control, replacement of potentially polluted plasmapheresis fluids, disinfecting the environment and replacing old sterile washing water with new sources were carried out in plasmapheresis unit. In conclusion, *R. pickettii* is a rare nosocomial infection that is responsible for the contamination of medical equipment, especially in hemodialysis, plasmapheresis devices and sterile solutions. Also, it is suggested that the role and importance of rare environmental bacteria as the causative agents of human infections should not be ignored in medical centers.

1. Introduction

Nosocomial bloodstream infections are defined as a group of infectious diseases in hospitalized patients after a 48-h hospitalization in medical centers. These infections can occur after postoperative wounds, urinary tract infections, and using intravascular devices by specific microorganisms such as coagulase-negative *staphylococci, Staphylococcus aureus,* methicillin-resistant *S. aureus* (MRSA), *Enterococcus* species, *vancomycin-resistant Enterococci, Escherichia coli*, *Bacteroides* species, and *Candida* species [1]. However, sometimes a group of rare environmental microbes such as *Ralstonia* species causes these types of infections. *Ralstonia pickettii*, non-fermentative Gram-negative bacteria was first isolated in 1970 and named after Ericka Ralston, an American bacteriologist [1,2]. Ralstonia not only is a highly resistant bacterial species in natural environments but is also introduced as a rare opportunistic agent in hospitals and medical centers. Moreover, this bacterial species is not considered a part of the human normal flora. According to the studies, this bacterium can contaminate many injection solutions and hospital water sources, as well as cause bacteremia, urinary tract infections, sepsis, septic shock, and even death in infants, autoimmune disease, or immunodeficiency patients [2]. Although bloodstream infection caused by *R. pickettii* is very rare in this study we identify and report rare case of *Ralstonia pickettii* bloodstream infection in the patient with Guillain-Barre syndrome under plasmapheresis.

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2. Case presentation

A 15 -year-old boy was referred for admission to the neurology center of the teaching hospital of Shiraz, Iran for inability to walk, lower extremity muscle weakness, and tingling in the feet. Physical exam presented hyporeflexia and initial laboratory exam documented White Blood Cell (WBC) 8.1 $\times$ 10^9 cells/L, Hemoglobin (Hb) 15.6 g/dL, neutrophils 66.9 %, and *Blood Urea Nitrogen* (*BUN*) 23 mg/dL and creatinine 0.6 mg/dl rates. Also, Cerebrospinal fluid (CSF) analysis revealed without RBC, Glucose 68 mg/dL, lactate dehydrogenase (LDH) 29 U/L, and without microorganisms existing in Gram stain exam. One week after hospitalization, biochemistry results presented constant BUN 23 mg/dL and calcium 10.5 mg/dL levels, but the creatinine 0.6 mg/dl rate continued to decrease. Moreover, the amount of Hb 13.5 g/dL suddenly decreased, and serological tests showed high C-Reactive Protein (CRP) quantitative 8 mg/L results. However, a double-lumen tube (DLT) was placed for the patient and he underwent plasmapheresis one time. Moreover, a few hours after plasmapheresis the patient was also given Intravenous immune globulin (IVIG) 0.4 g/kg/day for 5 days. During hospitalization and after plasmapheresis, about 24–48 h later, the patient developed to severe fever besides shivering. Hence blood culture was ordered and *M*eropenem (1gr/Q8h/IV) prescribed for prophylaxis through this period, until blood infection and antibiotic susceptibility test results were discovered. Additionally, the determination of Procalcitonin (PCT) 2.44 ng/mL and CRP quantitative 13 mg/L results indicated probably occurrence of a systemic infection. After 24 h, from blood cultures capturing, using the BACT/ALERT®3D instruments, blood culture showed positive results. Besides the DLT culture was infected with a rare microorganism. To identify the mentioned microorganism, the content of BACTEC bottles was extracted for bacteriological culture and exam. After 48h the laboratory results indicated pinpoint colonies without hemolysis after a 72-h incubation at 35 °C on blood agar, non-fermenting colonies on Mac Conkey Agar, aerobic Gram-negative bacilli with oxidase positive reactions, able to urea hydrolysis, and positive for gelatin liquefaction. Furthermore, positive motility, resistance to Colistin (10 μg disk), Polymyxin B (300 U disk) and inability to lysine decarboxylation. This characteristic was a sign of bacteremia with *R. pickettii*. In addition, tip catheter cultures results disclosed *R. pickettii* infections. Although there is no specific instruction for an antibiotic susceptibility test for *R. pickettii*, *Kirby–Bauer* disk diffusion method was performed according to Clinical and Laboratory Standard Institute (CLSI) 2021 guidelines [3,4]. Besides, the antibiotic selection was according to antibiotics that are commonly prescribed in our medical centers and *M*eropenem (1gr/Q8h/IV) prescribed, 4–5 days from the onset of fever to the laboratory results, for treatment. After that, antibiotic susceptibility test results reports presented the susceptibility of *R. pickettii* to *Ampicillin-Sulbactam (10/*10 μg*), Cefepime (*30 μg*), Cephalexin (*30 μg*), Ciprofloxacin (*5 μg*), Ceftriaxone (*30 μg*), Cefotaxime (*30 μg*), Imipenem* (10 μg), *Levofloxacin (*5 μg*), Piperacillin/Tazobactam (100/*10 μg*), Co-Trimoxazole_*SXT (25 μg*), Tetracycline (*30 μg*),* and Tigecycline (15 μg). Also, this strain showed resistant to *Amikacin (*30 μg*), Ampicillin (*10 μg*), Amoxicillin-clavulanic acid* (20/10 μg), *Ceftazidime (*30 μg*) Cefixime (*5 μg*), Chloramphenicol* (30 μg), *Gentamicin (*10 μg*),* and *Tobramycine (*10 μg*)*. According to antibiotic susceptibility test *reports*, *M*eropenem prescribing stopped and *Ciprofloxacin (*5 μg*)* was prescribed for the patient. Fortunately, after starting antibiotic treatment, blood culture results reported no growth after 5 days. After four weeks of hospitalization, significant changes were observed in the results of the hematology and biochemistry tests. For example, a stable decrease in Hb 13.2 g/dL rates, increase in the different index such as Aspartate Aminotransferase (AST/SGOT) 79 U/L, Alanine Aminotransferase (ALT/SGPT) 144 U/L, Gamma-Glutamyl Transferase (GGT) 173 U/L, and A*lkaline Phosphatase* (ALP) 1667 U/L ranges in the blood specimens. The viral tests according to the chemiluminescence method disclosed non-reactive results for HBs Ag, HCV Ab, HIV Ag, and HIV Ab**.** In addition, RT-PCR method for *coronavirus* (*COVID-19*) had negative results. After four weeks of hospitalization, he got jaundiced with bilirubin increasing and the results of the Anti-HAV (IgM Antibodies) test were positive and the patient was infected with hepatitis A during hospitalization. URSOBIL (300 mg/BID/Po) was prescribed at this time. Biochemistry tests such as the amount of total bilirubin (4.5 mg/dL), AST and ALT (700–1000 U/L) have increased. Also, we assumed that Hepatitis A infection in our patient was probably a hospital infection. Since during hospitalization the ALT and AST or the GGT and Alkaline phosphatase (ALP) were more significantly elevated probably raising the opinion of biliary obstruction cause jaundice that may due to complication of meropenem prescribing. Besides rheumatology and serology exam such as Anti-Nuclear Antibody (ANA), Anti ds DNA, C3 and C4 Complement blood test, and Coombs Wright (with Brucella immunocapture assay method) had negative results. During the disease, the patient was diagnosed with severe thrombocytopenia. Hence, a malignancy workup was done, and a bone marrow sample was taken from the patient. Peripheral Blood Smear (PBS) reported normal WBC count, without polymorphonuclear leukocyte (PMN) toxic granulation, PMN dominant in WBC diff, lacking vacuolization in PMN, normocytic normochromic anemia, fragmented RBC less than 1 %, and thrombocytopenia with platelet count about 78000 that might be due to meropenem administration. Echocardiography results exhibited good Left Ventricular (LV) systolic function, left aortic arch, no coarctation of the aorta (COA), good right ventricular (RV) systolic function. Also, the patient did not have Shwachman-Diamond Syndrome (SDS). In addition, a trivial amount of pulmonic regurgitation (PR), no pulmonary hypertension, and trivial tricuspid valve regurgitation. The final diagnosis was Guillain-Barré syndrome, and the patient was treated with plasmapheresis once during hospitalization. Additionally, the patient was also given Intravenous immune globulin (IVIG). Fortunately, in our study, R. picketti bacteremia was well treated by ciprofloxacin. Also, in this study, the plasmapheresis device was identified as a possible source of contamination. Hence, after reporting the infection occurrence to the hospital infection control unit, initial and possible measures such as device infection control, replacement of potentially polluted plasmapheresis fluids, disinfecting the environment and replacing old sterile washing water with new sources were carried out in plasmapheresis unit.

3. Discussion

Medical devices such as hemodialysis and plasmapheresis devices in the hospital play a very important role in the transmission and causing nosocomial bloodstream infections in the patient with various autoimmune or immunodeficiency disorders. In this study, we identify and report rare case of *R. pickettii* bloodstream infection in patient with Guillain-Barre syndrome under plasmapheresis. According to older taxonomy, Ralstonia is classified as one of the species in the genus Pseudomonas but today reclassified in the family Burkholderiaceae, rRNA group II, and genus Ralstonia based on DNA-rRNA hybridization. Although the virulence factors and pathogenesis of Rastonia are not completely clear, different strains have been isolated from different patients [4]. For instance, R. mannitolilytica *and* R. insidiosa have been recovered from the sputum of the cystic fibrosis patients [5,6], recurrent meningitis [7], peritoneal fluid infection [8], and catheter-related bacteremia [9]. *R. pickettii* was introduced as a type species and rarely associated with human infections. As well, it is known as a putative nosocomial infection and isolated from various human clinical specimens. This bacterial species is accountable for hospital germ-free solutions contamination such as sterile saline, intravenous fluids, chlorhexidine, heparin, distilled water, hemodialysis water, and respiratory care solutions [10–15]. According to different reports, *R. pickettii* is associated with native valve endocarditis [16], neonatal sepsis [17], meningitis [18], vertebral osteomyelitis [19], and community-acquired pneumonia [20]. However, it causes bacteremia in hemodialysis, blood-transplant, and cancer patients [21,22]. Although different

studies mentioned that the main population at risk for *R. pickettii* bloodstream infection are immunocompromised patients, our results indicated patients with an autoimmune disorder under plasmapheresis such as Guillain-Barré syndrome are also susceptible to *R. pickettii* bacteremia. In this syndrome, the human immune system attacks the nervous systems and causes weakness in the hands, feet, and consequently paralyzing the whole of the body. In this situation, IVIG and plasmapheresis may be prescribed to diminish the symptoms of the disease. Transmission of infectious agents to the blood following the placement of an intravascular catheter is one of the risks factors during plasmapheresis. Also, the nosocomial *R. pickettii* bacteremia occurrence is the most adverse event during plasmapheresis, especially after the use of a central venous catheter or at the catheterization sites. However, there are no standard therapeutic guidelines for the treatment of *R. pickettii* infections. Some studies have shown that this agent has been treated successfully by aminoglycosides and carbapenems. Similarly, in this study, our strain was well treated after C*iprofloxacin* prescribing. Finally, because Ralstonia can pass through the 0.2-μm filters, persevere in harsh environmental conditions, and participate in biofilm formation in plasmapheresis devices, it can be considered the risk factors and main source of the contamination for patients in hemodialysis and plasmapheresis departments. As a result, it is suggested that the role and importance of rare environmental bacteria as the causative agents of human infections should not be ignored in terms of laboratory diagnosis and treatment.

4. Conclusion

In this study, we reported a bloodstream infection caused by *R. pickettii* in a patient with Guillain-Barre disease. *R. pickettii* bacteremia in autoimmune patients during plasmapheresis is rarely reported. Health workers and physicians must consider the nosocomial infection of Ralstonia in hospitalized autoimmune patients. Also, during plasmapheresis or hemodialysis, sterility of the medical devices, hospital solutions, catheter, hand hygiene, and surgeries equipment must be considered especially for immunocompromised, autoimmune disorder, and infant patients. Furthermore, the role and importance of rare environmental bacteria as the causative agents of human infections should not be ignored in terms of laboratory diagnosis and clinical treatment.

Ethical approval

This case report is a part of the study conducted in Shiraz University of Medical Sciences, Shiraz, Iran with ethics code IR. SUMS.MED. REC.1399.644 and research code 21863 that during its implementation, we came across this case and reported.

Funding

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Consent

In this study, the personal information of the patient was ignored and the information of the created disease was used for scientific investigations. Also, general consent was obtained from the patient's parents.

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Ethical statement

This case report is a part of the study conducted in Shiraz University of Medical Sciences, Shiraz, Iran with ethics code IR. SUMS.MED. REC.1399.644 and research code 21863.

Data availability

There is no available data as this work used available literature.

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CRediT authorship contribution statement

Farhad Moradi: Writing – review & editing, Writing – original draft, Validation, Resources, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Mahrokh Rajaee behbahani:** Methodology, Investigation, Data curation. **Javid Gorginpour:** Funding acquisition, Investigation, Methodology, Resources. **Asiyeh Dezhkam:** Visualization, Validation, Supervision, Project administration. **Nahal Hadi:** Visualization, Validation, Supervision.

Declaration of competing interest

None.

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References

[1] Bergey DH. 1860-1937. And John G holt. Bergey's manual of determinative bacteriology. ninth ed. Philadelphia: Lippincott Williams & Wilkins; 2000.
[2] Segrelles-Calvo G, Sánchez Hernández A, Rey L. Bilateral pneumonia due to Ralstonia pickettii in immunocompetent patient. Med Clin 2016;147(11):516–7. https://doi.org/10.1016/j.medcli.2016.06.037.
[3] CLSI. Performance standards for antimicrobial susceptibility testing, M100. 31st ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2021.
[4] Procop GW, Church DL, Hall GS, Janda WM. Koneman's color atlas and textbook of diagnostic microbiology. Jones & Bartlett Publishers; 2020.
[5] Coenye T, Vandamme P, LiPuma JJ. Infection by *Ralstonia* species in patients with cystic fibrosis: identification of *R. pickettii*, and *R. mannitolilytica* by polymerase chain reaction. Emerg Infect Dis 2002;8:692–6. https://doi.org/10.3201/eid0807.010472.
[6] Coenye T, Goris J, De Vos P, Vandamme P, LiPuma JJ. Classification of Ralstonia pickettii-like isolates from the environment and clinical samples as Ralstonia insidiosa sp. nov. Int J Syst Evol Microbiol 2003 Jul;53(Pt 4):1075–80. https://doi.org/10.1099/ijs.0.02555-0.PMID:12892129.
[7] Vaneechoutte M, De Baere T, Wauters G, et al. One case each of recurrent meningitis and hemoperitoneum infection with *Ralstonia mannitolilytica*. J Clin Microbiol 2001;39:4588–90. https://doi.org/10.1128/JCM.39.12.4588-4590.2001.
[8] Dotis J, Printza N, Orfanou A, Papathanasiou E, Papachristou F. Peritonitis due to Ralstonia mannitolilytica in a pediatric peritoneal dialysis patient. New Microbiol 2012 Oct;35(4):503–6. Epub 2012 Oct 1. PMID: 23109020.
[9] Gröbner S, Heeg P, Autenrieth IB, Schulte B. Monoclonal outbreak of catheter-related bacteraemia by Ralstonia mannitolilytica on two haemato-oncology wards. J Infect 2007;55(6):539–44. https://doi.org/10.1016/j.jinf.2007.07.021. Epub 2007 Sep 19. PMID: 17881058.
[10] Labarca JA, Trick WE, Peterson CL, Carson LA, Holt SC, Arduino MJ, Meylan M, Mascola L, Jarvis WR. A multistate nosocomial outbreak of Ralstonia pickettii colonization associated with an intrinsically contaminated respiratory care solution. Clin Infect Dis 1999;29(5):1281–6. https://doi.org/10.1086/313458.PMID:10524976.
[11] Marroni M, Pasticci MB, Pantosti A, Colozza MA, Stagni G, Tonato M. Outbreak of infusion-related septicemia by Ralstonia pickettii in the oncology department. Tumori 2003;89(5):575–6. https://doi.org/10.1177/030089160308900528.PMID:14870792.
[12] Chetoui H, Melin P, Struelens MJ, Delhalle E, Nigo MM, De Ryck R, De Mol P. Comparison of biotyping, ribotyping, and pulsed-field gel electrophoresis for

investigation of a common-source outbreak of Burkholderia pickettii bacteremia. J Clin Microbiol 1997;35(6):1398–403. https://doi.org/10.1128/jcm.35.6.1398-1403.1997. PMID: 9163452; PMCID: PMC229757.

[13] Maroye P, Doermann HP, Rogues AM, Gachie JP, Mégraud F. Investigation of an outbreak of Ralstonia pickettii in a paediatric hospital by RAPD. J Hosp Infect 2000;44(4):267–72. https://doi.org/10.1053/jhin.1999.0691.PMID:10772834.

[14] Strateva T, Kostyanev T, Setchanova L. Ralstonia pickettii sepsis in a hemodialysis patient from Bulgaria. Braz J Infect Dis 2012;16(4):400–1. https://doi.org/10.1016/j.bjid.2012.06.010. PMID: 22846135.

[15] Pellegrino FL, Schirmer M, Velasco E, de Faria LM, Santos KR, Moreira BM. Ralstonia pickettii bloodstream infections at a Brazilian cancer institution. Curr Microbiol 2008;56(3):219–23. https://doi.org/10.1007/s00284-007-9060-1. Epub 2007 Nov 10. PMID: 17994262.

[16] Orme J, Rivera-Bonilla T, Loli A, Blattman NN. Native valve endocarditis due to Ralstonia pickettii: a case report and literature review. Case Rep Infect Dis 2015:324675. https://doi.org/10.1155/2015/324675. Epub 2015 Jan 11. PMID: 25648998; PMCID: PMC4306225.

[17] Sharma D, Sharma P, Soni P, Gupta B. Ralstonia picketti neonatal sepsis: a case report. BMC Res Notes 2017;7(1):10. https://doi.org/10.1186/s13104-016-2347-1. PMID: 28061799; PMCID: PMC5219797.

[18] Heagney MA. An unusual case of bacterial meningitis caused by *Burkholderia pickettii*. Clin Microbiol Newsl 1998;15; 20(12):102–3.

[19] Wertheim WA, Markovitz DM. Osteomyelitis and intervertebral discitis caused by Pseudomonas pickettii. J Clin Microbiol 1992;30(9):2506–8. https://doi.org/10.1128/jcm.30.9.2506-2508.1992.

[20] Rammaert B, Borand L, Goyet S, Te V, Hem S, Guillard B, Vong S. Ralstonia pickettii community-acquired pneumonia in Cambodia [Correspondence]. Int J Tubercul Lung Dis 2010;1.14(12):1653–4.

[21] Pellegrino FL, Schirmer M, Velasco E, De Faria LM, Santos K, Moreira BM. Ralstonia pickettii bloodstream infections at a Brazilian cancer institution. Curr Microbiol 2008;56(3):219–23. https://doi.org/10.1007/s00284-007-9060-1.

[22] Tejera D, Limongi G, Bertullo M, Cancela M. Ralstonia pickettii bacteremia in hemodialysis patients: a report of two cases. Revista Brasileira de terapia intensiva 2016;28:195–8. https://doi.org/10.5935/0103-507X.20160033.