

Ralstonia Pickettii Bacteremia

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Introduction

Ralstonia Pickettii is an aerobic, gram negative non-fermentative bacterium. Presumed to be an environmental organism it has been reported from soil, water and plants [1]. Generally not associated with native human flora, it can be a commensal in the upper respiratory tract and causes disease in patients with waning immunity [1].

As mentioned in literature *R. pickettii* has been reported to cause respiratory tract infections, meningitis, peritonitis and sepsis [1-4]. Transmission may occur due to contaminated medical devices or solutions generally encountered in health care facilities. *R. pickettii* has been reported to cause outbreaks also [5]. We present three case reports of *R. pickettii* bacteremia and a brief review of literature. Though a case of bacteremia has been reported very recently from India [6], this is, to the best of our knowledge, the first case series from India.

Case Report 1

A forty year old foreign national was admitted for evaluation of refractory Diffuse Large B-cell lymphoma. He was suffering from fever and weight loss for past 1 month and had deep mucosal ulcers. Blood parameters indicated hemoglobin 10.3 gm/dl, red blood cell count $3.3 \times 10^6/\mu\text{l}$, total leucocyte count 3000 cells/ μl , platelets 6000/ μl , urea 78 mg/dl and creatinine 1.7 mg/dl. The patient was shifted on Mini BEAM chemotherapy. On day 2, he developed sudden hypotension and was shifted to the intensive care unit and was ventilated. A central line was inserted and he was put on vasopressor support. Intravenous meropenem 1 gm i.v 8 hourly was started empirically. Gradually his parameters stabilized though the neutropenic blood picture continued to persist. Patient deteriorated significantly on day 20. Fresh nodular opacities were visualized radiologically and endotracheal (ET) secretion and paired blood samples were sent for culture. Serum procalcitonin level was 12.7 ng/ml. Endotracheal and blood culture samples both grew nonlactose fermenting colonies on Macconkey agar, ET secretion growing with a colony count of 10^6 CFU/ml. Direct Time to Positivity (DTP) for the paired blood samples was more than 2 hours. The colonies were catalase and oxidase positive. The isolate was identified as *R. pickettii*. Identification and antibiotic susceptibility was done on VITEK 2 compact system (Biomerieux, USA). It was found sensitive to ceftazidime, ciprofloxacin and trimethoprim-sulfamethoxazole. The patient was put on i.v ceftazidime 1 gm/day. However his renal parameters deteriorated further and on day 23, the patient suffered a sudden cardiac arrest and could not be resuscitated.

Case Report 2

A 30 year old case of acute lymphoblastic leukemia was admitted for allogenic stem cell transplant. On admission hemoglobin was 4 gm/dl, total leucocyte count 800 cells/ μl and platelets 32000/ μl . The

patient was started on a conditioning regimen of Melphalan and Fludarabine through a hickmann catheter. Stem cell transplant was performed on Day 11 with patient receiving Graft Versus Host Disease (GVHD) prophylaxis of Cyclosporine and Methotrexate. On day 14, the patient developed high grade fever with diarrhea and vomiting. i.v metronidazole 7.5 mg/kg and i.v meropenem 1 gm 8 hourly along with supportive fluid therapy were initiated. Paired blood samples, taken from catheter and peripheral site flagged positive on BD Bactectm systems DTP was more than two hours. Identification of the isolate as *R. pickettii* was carried on the VITEK 2 system. Our isolate was sensitive only to cefepime and ciprofloxacin according to the Vitek report. Treatment was changed accordingly. However the condition of the patient worsened due to severe hypokalemia. In spite of all the rehydration and supportive measures, the patient succumbed to multi organ failure.

Case Report 3

A 19 year old thalassemic patient was admitted for evaluation of skin rashes and severe diarrhea. Two months earlier, she had undergone an allogenic stem cell transplant. Rashes were present on her back, trunk and arms. A Hickmann catheter was in situ. Hematological investigations revealed hemoglobin 13 gm/dl, total leucocyte count 13.9×10^3 cells/ μl and platelets 13.2×10^3 cells/ μl . Gastric biopsy revealed mucosal edema with fibrinous exudates consistent with the diagnosis of gut GVHD. The patient was put on immunosuppressive drugs cyclosporine and solumedrol. Antibiotics given empirically were i.v meropenem 1 gm i.v 8 hourly and metronidazole i.v 7.5 mg/kg. On day 10, the patient had spike of fever measured to be 102°C . His total leucocyte count was 16×10^3 cells/ μl and platelets dipped to 84000 cell/ μl . Paired blood samples flagged positive on BD BACTECTM.system grew non lactose fermenting, nonpigmented smooth colonies. These were identified as *R. pickettii* by Vitek 2 compact. The patient was put on ciprofloxacin i.v 400 mg 8 hourly as per susceptibility report. The patient responded to the treatment and was discharged on Day 21.

Discussion

The classification of *R. pickettii* has undergone many taxonomic changes. Previously identified as Burkholderia, it now has an independent status [2] Emerging as an important pathogen in health care facilities, its causative role in patient morbidity cannot be ignored.

R. pickettii has been described to cause pulmonary infections especially in cystic fibrosis patients [1] In one study, *R. pickettii* was isolated from 38 sputum samples [2] As described in our first case, *Ralstonia* was isolated from the endotracheal secretions and subsequently from blood. Persistent colonization of the airways in this immunocompromised individual by this organism seems to be a plausible hypothesis which may have led to secondary bacteremia.

In our second and third cases, *R. pickettii* was isolated from twin sets of blood culture in absence of any identifiable infective foci. Heparin flush was cultured to look for the source but was found to be sterile. There was a Hickmann catheter in situ which could not be sent

for culture. DTP was positive suggesting central line associated infection. *R. pickettii* sepsis has been reported in literature where contaminated intravenous solutions, medical devices like port-a-cath and central lines [4,7] were incriminating foci (Table 1).

Journal	Year publishing	Reference number	No. patients	Source bacteremia(if reported)	Antibiotic sensitivity pattern	Immune status	Outcome
Journal of clinical Microbiology	1985	[7]	15	Chlorhexidine aqueous solution	Sensitive to ampicillin, cefazolin, tetracycline, trimethoprim-sulphamethoxazole	Not mentioned	survived
Clinical Infectious Diseases	1996	[5]	46	Intravenous Ranitidine solution	Not mentioned	Not mentioned	survived
Journal of clinical Microbiology	1998	[8]	3	Port-a-cath	Sensitive to imipenem and ceftazidime	compromised	survived
Journal of Pediatr Hematol Oncology	2005	[4]	2	Port-a-cath	Not mentioned	compromised (malignancy)	survived
Pediatr Infect Dis Journal	2005	[10]	18	Heparin flush	Not mentioned	Not mentioned	survived
Brazilian journal of infectious disease	2011	[9]	1	Dialysis system	Sensitive to piperacillin tazobactam, ciprofloxacin, ceftazidime, cefepime imipenem, meropenem and trimethoprim-sulphamethoxazole	Chronic kidney disease	survived
Indian Journal of medical microbiology	2014	[6]	1	Not mentioned	Sensitive to colistin and tigecycline	compromised (malignancy)	survived
European journal of clinical microbiology and infectious diseases	2014	[11]	Multiple case reports [8-11]	Multiple reports case	Multiple case reports	compromised	All survived

Table 1: *Ralstonia pickettii* Bacteremia – Brief Review of Literature

Antibiotics which have activity against *R. pickettii* are piperacillin-tazobactam, ceftriaxone, cefepime, levofloxacin, ciprofloxacin, cotrimaxazole and meropenem [12]. Also it has been researched that this bacteria produces many beta-lactamases. An imipenem hydrolyzing enzyme OXA-60 has been isolated from *Ralstonia* [1]. Recently,

Khajuria et al. have reported VIM-2 metallo beta lactamase enzyme from a *R. pickettii* isolate in blood [6].

Table 2 gives the MIC breakpoints of all the isolates in our report which have been interpreted according to CLSI guidelines.

Antibiotics	isolate 1	interpretation	isolate 2	interpretation	isolate 3	interpretation
Amikacin	≥64	R	≥64	R	≥64	R
Gentamicin	≥16	R	≥16	R	≥16	R
Ceftazidime	2	S	16	R	1	S
Cefepime	16	I	2	S	1	S
Ciprofloxacin	1	S	≤0.25	S	≤0.25	S
Trimethoprim-sulphamethoxazole	≤20	S	≤20	S	≤20	S
Piperacillin-tazobactam	≥128	R	≥128	R	16	S
Imipenem	≥16	R	8	R	1	S
Meropenem	≥16	R	≥16	R	4	I

Colistin	≥16	R	≥16	R	≥16	R
†MIC—minimum inhibitory concentration R-resistant, S-sensitive, I-intermediate						

Table 2: Comparison of MIC[†] breakpoints of antibiotics for three isolates of *Ralstonia pickettii*, (µg/ml)

Also, it is worthwhile mentioning that isolation of *R. pickettii* from blood in three patients cannot be termed as an outbreak. All the patients were admitted in different time periods. Moreover the antimicrobial susceptibility of all these isolates were variable [13-15].

Novel gram negative bacilli like *Ralstonia* are increasingly being isolated from intensive care and oncology units. All our cases could be line associated. An attempt to look into the probable cause of these isolates was not diagnostic and was inconclusive. However infection control protocols have been reinstated and we are vigilant for any new cases. The limitation of our study is the inability to sequence the three strains. This would have shed light on the existing hospital ward epidemiology. Previously being reported as *Burkholderia* species and recently as *Ralstonia* emphasizes the observation that identification is not easy and misdiagnosis is an issue. In developing countries, where sophisticated Microbiology laboratories are far from reality, it is immensely difficult to correctly identify these non fermenters. We have used Vitek GN card for identification and ASTN281 panel for antimicrobial susceptibility. Reproducibility of the Vitek 2 compact system is well established now. Knowledge about local epidemiology and these novel bacteria has immense significance in designing infection control policies and antibiotic stewardship programmes.

Studies like ours can create awareness and help in reducing antibiotic resistance, hospital associated infections and improve patient outcome.

References

1. Coenye T, Vandamme P, LiPuma J (2002) Infection by *Ralstonia* Species in Cystic Fibrosis Patients: Identification of *R.pickettii* and *R.mannitolilytica* by Polymerase Chain Reaction. *Emerging Infectious Diseases* 7: 692-696
2. Baere TD, Steyaert S, Waters G, Vos P, Goris J, Coenye T, et al. (2001) Classification of *Ralstonia Pickettii* biovar 3/'thomasii' strains (Pickett 1994) and of new isolates related to nosocomial recurrent meningitis as *Ralstonia mannitolilytica* sp.nov. *Int J Syst Evol Microbiol* 51: 547-558
3. Dotis J, Printza N, Orfanou A, Papathanasiou E, Papachristou F (2012) Peritonitis due to *Ralstonia mannitolilytica* in a pediatric peritoneal dialysis patient. *New Microbiol* 35: 503-506.
4. Kismet E, Atay AA, Demirkaya E, Aydin HI, Aydogan H, et al. (2005) Two cases of *Ralstonia Pickettii* bacteremias in a pediatric oncology unit requiring removal of the Port-A-Caths. *J Pediatr Hematol Oncol* 27: 37-38.
5. Fernandez C, Wilhelmi I, Andradas E, Gaspar C, Gomez J, et al. (1996) Nosocomial outbreak of *Burkholderia pickettii* Infection Due to a Manufactured Intravenous Product Used in Three Hospitals. *Clinical Infectious Diseases* 22: 1092-1095
6. Khajuria A, Praharaj AK, Grover N, Kumar M (2014) Emergence of VIM-2 metallo-beta-lactamase producing *Ralstonia Pickettii* clinical isolate in India. *Indian J Med Microbiol* 32: 191-193.
7. Verschraegen G, Claeys G, Meeus G, Delanghe M (1985) *Pseudomonas pickettii* as a cause of pseudobacteremia. *J Clin Microbiol* 21: 278-279.
8. van Pelt C, Verduin CM, Goessens WH, Vos MC, Tümmeler B, et al. (1999) Identification of *Burkholderia* spp. in the clinical microbiology laboratory: comparison of conventional and molecular methods. *J Clin Microbiol* 37: 2158-2164.
9. Hansen W, Glupczynski G, Yourassowsky E (1982) Infections a *Pseudomonas pickettii*. *Med Mal Infect* 12: 507-511
10. Chomarat M, Lepape A, Riou JY, Flandrois JP (1985) [*Pseudomonas pickettii* septicemia]. *Pathol Biol (Paris)* 33: 55-56.
11. Poty F, Denis C, Baufine-Ducrocq H (1987) Nosocomial *Pseudomonas pickettii* infection. Danger of the use of ion-exchange resins. *Presse Med* 16: 1185-1187.
12. Hsueh Po-Ren, Teng Lee-Jene, Pan Hui-Ju, Chen Yu-Chi, Sun Chun-Chuan, et al. Outbreak of *Pseudomonas fluorescens* bacteremia among Oncology Patients. *Journal Of Clinical Microbiology*.1998; vol 36(10): 1914-2917
13. Strateva T, Kostyanov T, Setchanova L (2012) *Ralstonia Pickettii* sepsis in a hemodialysis patient from Bulgaria. *Braz J Infect Dis* 16: 400-401.
14. Kimura AC, Calvet H, Higa JJ, Pitt H, Frank C, et al. (2005) Outbreak of *Ralstonia Pickettii* bacteremia in a neonatal intensive care unit. *Pediatr Infect Dis J* 24: 1099-1103.
15. Ryan MP, Adley CC (2014) *Ralstonia* spp.: emerging global opportunistic pathogens. *Eur J Clin Microbiol Infect Dis* 33: 291-304.