

***Ralstonia mannitolilytica* bacteremia in a maintenance hemodialysis patient**Sreevidya Subramanian¹, S Venkatesh Rajkumar², M A Thirunarayan¹, Debashree Samal¹From ¹Department of Microbiology, ²Department of Nephrology, Apollo Speciality Hospitals, Chennai, Tamil Nadu, India**Correspondence to:** Dr. Sreevidya Subramanian, Department of Microbiology, Apollo Speciality Hospitals, Chennai, Tamil Nadu, India. E-mail: docsreevidya@gmail.com

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ABSTRACT

Ralstonia mannitolilytica is a nonfermentative, Gram-negative bacterium isolated infrequently from clinical samples. It is widely distributed in nature, being a frequent contaminant in water supplies. It is increasingly identified as an opportunistic pathogen in nosocomial infections, especially among immunosuppressed patients. It has also been implicated in common source nosocomial infection outbreaks due to the addition of contaminated water to parenteral fluids and to medical equipment presumed to be sterile. True bacteremia with the organism, however, cannot be ruled out, especially if it is isolated repeatedly from the same patient within 3 successive days from blood cultures. A 22-year-old Ethiopian male presented to us in December 2015 with fever with chills and rigor, vomiting, and headache. He was a known end-stage renal disease patient on thrice per week hemodialysis through a tunneled hemodialysis catheter for the past 1 year. He had an episode of catheter-related blood stream infection in October-November 2015 and was treated at a multispeciality hospital with parenteral antibiotics (piperacillin-tazobactam) for 2 weeks (for growth of *Pseudomonas aeruginosa* in blood cultures) during the same admission phase. The tunneled catheter was not removed then and lock therapy was used and the patient improved gradually with antibiotics. During the current admission, three blood culture sets (aerobic and anaerobic), one set from the dialysis line and two from the peripheral lines were submitted to microbiology laboratory. Blood cultures (one bottle from each of the three sets) flagged positive. The blood culture sent from the hemodialysis line was the first to flag positive 12 h after it was loaded onto the BACTEC 9050 system. This was followed by the aerobic and anaerobic bottles from the peripheral lines. The preliminary Gram-stain showed Gram-negative bacilli and the cultures grew Gram-negative organisms. The organism was identified as *R. mannitolilytica* by the Vitek 2C. Disc diffusion (CLSI, 2015) was done for the various antibiotics, and there was a 6 mm resistant zone for the following panel tested: Gentamicin, cotrimoxazole, aztreonam, amikacin, ceftriaxone, cefotaxime, cefepime, ceftazidime, and carbapenems; the organism was intermediate to piperacillin-tazobactam (17 mm) and was sensitive to and cefoperazone-sulbactam (23 mm). In our set up, this was the first case of *R. mannitolilytica* isolated as a significant pathogen in a case of true bacteremia. *R. mannitolilytica* can thus cause true bacteremia as well in addition to just being an environmental contaminant. Early recognition of the infection helps in instituting appropriate antibiotic with complete resolution of the infection. In our case report, the prompt report of microbiology department enabled us to treat the patient on time with appropriate antibiotic and also prevented the premature removal of the tunneled catheter. The problems caused by this bacterium occur rapidly and disease progression is fast; therefore, *R. mannitolilytica* infections should draw sufficient attention from clinical physicians and bacteriology workers to respond to the resulting severe consequences.

Key words: *Ralstonia mannitolilytica*, True bacteraemia, Treatment guidelines

R*alstonia mannitolilytica* is a nonfermentative, Gram-negative bacterium isolated infrequently from clinical samples. The novel genus *Ralstonia* includes three main pathogenic species: *Ralstonia pickettii*, *Roseomonas gilardii*, and *Roseomonas basiliensis* [1]. *R. pickettii* biovar 3/“*thomassii*” was shown to represent a separate species, *R. mannitolilytica* [2]. It is widely distributed in nature, being a frequent contaminant in water supplies. It is increasingly identified as an opportunistic pathogen in nosocomial infections [3,4], especially among immunosuppressed patients [5]. It has also been implicated in common source

nosocomial infection outbreaks due to the addition of contaminated water to parenteral fluids [6] and to medical equipment presumed to be sterile.

True bacteremia with the organism, however, cannot be ruled out, especially if it is isolated repeatedly from the same patient within 3 successive days from blood cultures.

CASE REPORT

A 22-year-old Ethiopian male presented to us in December 2015 with fever with chills and rigor, vomiting, and headache. He was a

known end-stage renal disease patient on thrice /week hemodialysis through a tunneled hemodialysis catheter for the past 1 year.

His significant medical history includes appendicitis requiring emergency admission for surgery at a nearby multispecialty hospital in October 2015.

Physical examination revealed mild pedal edema, temperature 100°F, and pulse 96/min with a blood pressure of 150/86 mm of Hg. There was no other remarkable finding in the general examination. His systemic examination revealed no other important finding except a tender epigastrium.

He had an episode of catheter-related bloodstream infection (CRBSI) in October-November 2015 and was treated at a multispecialty hospital with parenteral antibiotics (piperacillin-tazobactam) for 2 weeks (for growth of *Pseudomonas aeruginosa* in blood cultures) during the same admission phase. The tunneled catheter was not removed then and lock therapy was used and the patient improved gradually with antibiotics.

Recent investigations done during the present admission revealed a total leukocyte count of 20,000 cells/mm³ with a neutrophilic preponderance, hemoglobin 9.3 g/dl, urea 60 mg/dl, creatinine 6.3 mg/dl, sodium 141meq/l, potassium 4.7 meq/l, ALT 24 U/l, and alkaline phosphatase 114 U/l total protein 10.1 g/dl

Three blood culture sets (aerobic and anaerobic), one set from the dialysis line and two from the peripheral lines were submitted to microbiology laboratory. Blood cultures (one bottle from each of the three sets) flagged positive. The blood culture sent from the hemodialysis line was the first to flag positive 12 h after it was loaded onto the BACTEC 9050 system. This was followed by the aerobic and anaerobic bottles from the peripheral lines. The preliminary Gram-stain showed Gram-negative bacilli and the cultures grew Gram-negative organisms. The organism was identified as *R. mannitolilytica* by the Vitek 2C. Disc diffusion (CLSI 2015) was done for the various antibiotics, and there was a 6 mm resistant zone for the following panel tested: Gentamicin, cotrimoxazole, aztreonam, amikacin, ceftriaxone, cefotaxime, cefepime, ceftazidime, and carbapenems. The organism was intermediate to piperacillin-tazobactam (17 mm) and was sensitive to and cefoperazone-sulbactam (23 mm).

The patient was on piperacillin-tazobactam (4.5 g intravenous [IV] BD) initially, but the fever spikes were persisting. His fever decreased and he became afebrile after a change of therapy to cefoperazone-sulbactam (3 g of cefoperazone and 1 g of sulbactam/day in two divided doses) in accordance with the microbiology antibiotic sensitivity report. The patient responded well to the therapy (for 3 weeks) and was discharged in a hemodynamically stable condition with the tunneled catheter.

DISCUSSION

A limited number of cases of hospital outbreaks with *R. pickettii* biovar 3/"thomasi", i.e., *R. mannitolilytica* isolates have been reported in the literature. The first report [7] dealt with bacteremia due to parenteral fluids prepared with deionized water contaminated with "*P. thomasi*". An epidemic of *R. pickettii* involving 24 patients caused by contaminated saline

solution was reported [8]. Although no serious outbreaks related to *R. mannitolilytica* have been reported, so far the clinical importance of *R. mannitolilytica* may have been overlooked, possibly due to misidentification [8]. Most of these isolates are usually misdiagnosed as *P. aeruginosa* [9]. Our patient too had a previous hospitalization for CRBSI due to *P. aeruginosa* and it is quite possible that it could have been *R. mannitolilytica* misidentified as *Pseudomonas*. We, however, did not have the documents from the previous hospital and the susceptibility report of *Pseudomonas* was not available.

Our report is similar to the case setting reported by Gröbner et al. On monoclonal outbreak of catheter-related true bacteremia [10] due to *R. mannitolilytica* in hematology patients.

In our case, the organism isolated was unlikely to be a contaminant since it was isolated thrice on 3 consecutive days from the patient having the same antibiotic sensitivity pattern. Moreover, the patient responded dramatically when he was treated with the appropriate antibiotic in accordance with the sensitivity pattern. No possibilities could be hypothesized regarding the probable source of infection and the portal of entry for *R. mannitolilytica* in this patient as the patient presented to us for the first time and was getting hemodialysis from some other center till then. One potential portal of entry could be the water used for preparing dialysate solutions.

This case shows that *R. mannitolilytica* may be a more virulent pathogen than previously believed. Although no serious nonoutbreak-related infections have been described thus far, the clinical importance of *R. mannitolilytica* may have been overlooked, possibly due to misidentification as *Pseudomonas fluorescens*, *Burkholderia multivorans*, and/or *R. pickettii*, which are most often treated as contaminant [8]. Therefore, correct identification of this organism is of great importance, especially so in renal disease patients.

There have not been much reports of *R. mannitolilytica* bacteremia from India. The first of such reports was by Mukhopadhyay et al. [9] of a case of *R. mannitolilytica* in a post renal transplant patient. To the best of our knowledge, this is the first instance of reported *R. mannitolilytica* bacteremia in a hemodialysis patient with a CRBSI. We report our first case of *R. mannitolilytica* true bacteremia, in a dialysis patient with a tunneled catheter, in our newly opened hospital in South India where the patient was symptomatic because of the presence of this pathogen. Moreover, it was discharged in a stable condition after initiation of therapy.

Some limitations of the study were we could not gather correct information on whether the patient manipulated the dialysis line earlier (H/O IV drug abuse), and whether he maintained the long-term catheter with strict aseptic measures. The prior susceptibility reports could not be collected from the patient.

CONCLUSION

In our set up, this was the first case of *R. mannitolilytica* isolated as a significant pathogen in a case of true bacteremia. *R. mannitolilytica* can thus cause true bacteremia as well in

addition to just being an environmental contaminant. Early recognition of the infection helps in instituting appropriate antibiotic with complete resolution of the infection. In our case report, the prompt report of microbiology department enabled us to treat the patient on time with appropriate antibiotic and also prevented the premature removal of the tunneled catheter.

Currently, there are no clear treatment guidelines or CLSI breakpoints for identifying *R. mannitolilytica* infections. In the course of treatment, drug-susceptibility testing to adjust the use of antimicrobial agents is advocated. In addition, cotrimoxazole, ceftriaxone, and piperacillin/tazobactam are recommended for empirical treatment. Microbiological-detection personnel should pay attention to the slow growth of this bacterium. It is suggested that the growth condition should be determined after 48 h of culturing; otherwise, a missed diagnosis is likely to occur. The problems caused by this bacterium occur rapidly and disease progression is fast; therefore, *R. mannitolilytica* infections should draw sufficient attention from clinical physicians and bacteriology workers to respond to the resulting severe consequences.

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