

Providencia Rettgeri: An Emerging Nosocomial Uropathogen in an Indwelling Urinary Catheterised Patient

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ABSTRACT

Providencia rettgeri (*P. rettgeri*) is an ubiquitous organism but is seldom associated with human disease. We report the isolation of *P. rettgeri* from the urine sample of a 39-year-old male patient on prolonged Foley's catheterisation following a severe head injury. Identification of this organism was done by Matrix-Assisted Laser Desorption/Ionization Time of Flight Mass Spectrometry (MALDI-TOF) based systems. *P. rettgeri* is an emerging pathogen among long term catheterised patients. It reflects its ability to form biofilm on the surface of the indwelling catheter as well as the inherent urease producing property of the pathogen in question as a possible mechanism of pathogenesis.

Keywords: Antimicrobial resistance, Biofilm, Cephalosporins, Urinary tract infection

CASE REPORT

A 39-year-old man, with no significant travel history, no history of insect bites, or immunosuppression was admitted to Kasturba Hospital, Manipal on January 2016 with an alleged history of fall from a height of ~10 feet followed by loss of consciousness. There was no associated history of vomiting, convulsions, or frank nasal bleed. His Glasgow Coma Score at the time of admission was 5/15 (E₁V₁M₃) (E - Eye opening, V - Verbal response, M - Motor response) with bilateral pupils measuring 3 mm, and were non reactive. The patient was immediately catheterised using a Foley's catheter. Non contrast CT (Computed Tomography) scan of his brain revealed diffuse subarachnoid and intraventricular haemorrhage with diffuse cerebral oedema. The patient was initially managed conservatively with mechanical ventilation, anti oedema measures and vancomycin and cefoperazone-sulbactam for three weeks, followed by three weeks of ceftriaxone, amikacin and metronidazole as part of empirical therapy. The patient improved neurologically for the initial three weeks but later deteriorated. Hence, a repeat CT scan was warranted which revealed obstructive hydrocephalus. The patient was taken up for surgery and a ventriculoperitoneal shunt was placed with a therapeutic indication to alleviate the intracranial pressure. Subsequently, the patient did not improve. A shunt malfunction was detected and the shunt was revised.

Routine urine examination at that time from the indwelling Foley's catheter revealed triple phosphate crystals suggesting the presence of urea splitting bacteria and 8-10 WBCs / high power field. A urine sample from the same was sent to the laboratory for bacterial culture. The sample was cultured on 5% sheep blood agar and MacConkey agar and incubated at 37°C. The bacterial isolate analysis utilising the Vitek2 (bioMerieux, Hazelwood MO) phenotypic identification system revealed *P. rettgeri* with a colony count of >10⁵ CFU/ml. As *P. rettgeri* is an uncommon cause of urinary tract infection, the identity of the isolate was confirmed by MALDI-TOF. Antibiotic susceptibility, done using the Vitek MS (mass spectrometry) system, revealed that the isolate was resistant to ampicillin/amoxicillin: MIC >32, cefotaxime/ceftriaxone: MIC >64, cefuroxime: MIC >64, trimethoprim / sulphamethoxazole: MIC >320, amikacin: MIC >64, gentamicin: MIC >16, norfloxacin: MIC >4, cefoperazone-sulbactam: MIC >64, ceftazidime/cefepime: MIC >64, imipenem: MIC >16, and piperacillin-tazobactam: MIC >128.

Owing to the multidrug resistant nature of the isolate and considering it as a catheter-associated asymptomatic bacteriuria, the ongoing antibiotics were continued and a repeat urine sample was sought from a fresh Foley's catheter. It revealed the same organism with the same antibiogram. Subsequent to the revision of shunt procedure, the patient improved neurologically over a period of one month and antibiotics were taken off. In view of the aforementioned organism that was isolated, a midstream urine sample was sent after the removal of the catheter once the patient's condition stabilised. The culture was sterile after 36 hours of incubation, thus proving that *P. rettgeri* in this scenario resulted in asymptomatic bacteriuria due to prolonged catheterisation and not due to an ascending urinary infection. The patient was discharged in a stable condition, and showed progressive improvement on subsequent follow up visits to the hospital. Later when the culture revealed *P. rettgeri*, the catheter was changed and a repeat urine sample was sent from a fresh Foley's catheter which revealed the same organism with the same resistance pattern. Notwithstanding the report, and considering it as catheter associated asymptomatic bacteriuria, the ongoing treatment was not revised and the antibiotics were continued. Subsequent to the revision procedure, the patient improved neurologically over a period of one month. Urine sample sent after removal of catheter was sterile after 36 hours of incubation, thus proving that *P. rettgeri* in this scenario resulted in asymptomatic bacteriuria due to prolonged catheterisation and not an ascending urinary infection. The patient was discharged in a stable condition, and showed progressive improvement on subsequent follow up visits to the hospital.

DISCUSSION

Providencia represents a genus of urease producing, gram negative bacilli which although rare, are quite ubiquitous in the environment. *Providencia* species closely resemble *Proteus* and *Morganella* species. The genus *Providencia* encompasses five common species i.e., *P. alcalifaciens*, *P. rettgeri*, *P. stuartii*, *P. rustigianii*, and *P. heimbachae*. They are frequently isolated from wounds, respiratory tract and urinary tract (*P. alcalifaciens*, *P. rettgeri* and *P. stuartii*), stool of humans (*P. alcalifaciens*), poultry, faeces from reptiles (*P. rettgeri*), throat, perineum, axilla and blood of humans [1]. A report from Nepal in 2014, a cluster of surgical infections with regards to the isolation of *P. rettgeri*, demonstrated the presence

and significance of this organism in the Asia-Pacific region [2]. *P. rettgeri* has been implicated in the etiology of gastrointestinal illness in 1986, traveler's diarrhea in 2004, and ocular infection in 2006 [3-5]. *P. rettgeri* has also been implicated as a causative agent of "purple bag syndrome", where the enzymatic activity gives rise to a purple tinged urine [6].

With respect to antimicrobial susceptibility patterns, *P. rettgeri* is typically resistant to gentamicin and tobramycin but susceptible to amikacin [1]. However in the present study, we have found *P. rettgeri* was resistant to amikacin and gentamicin. Study conducted by Wie SH reported that 86% of the clinical isolates were resistant to amikacin and 71% of the isolates were resistant to gentamycin [7]. There have been scattered reports of Extended Spectrum Beta Lactamase (ESBL) producing *P. rettgeri* in Eastern Europe and New Delhi, and Metallo- β -lactamase-1 (NDM-1) producing *P. rettgeri* isolates in South America and Asia [8-10]. The NDM-1 gene produces of an enzyme called carbapenemase in *Providencia* species, which confers carbapenem resistance, along with other antibiotics [8]. Gentamicin and tobramycin resistance is common among *Providencia stuartii* and *Providencia rettgeri*, however both are partially susceptible to gentamicin. They also show sensitivity to ciprofloxacin, cephalosporins, carbapenems and amoxicillin-clavulanate, however a recent study of six years duration by Fass RJ et al., reported that the sensitivity of *Providencia* to ciprofloxacin has reduced from 100% to 46%; this slide down illustrates the potential for emerging resistance in this genus and the requirement for routine susceptibility tests [11].

The relationship between Catheter-Associated Asymptomatic Bacteriuria (CA-ASB) and Catheter-Associated Urinary Tract Infection (CA-UTI) and other clinical outcomes remains unclear and complicates our assessment of the importance of CA-ASB. The vast majority of patients with CA-ASB do not progress to CA-UTI as in our patient and factors that trigger a symptomatic event in patients with asymptomatic bacteriuria are not known. Thus, even though the presence of CA-ASB is presumably necessary for the development of CA-UTI, the development of urinary symptoms must require some facilitating event(s), such as tissue invasion, that we do not yet understand [12]. Thus, the repeated isolation of *P. rettgeri* from the second urine culture suggested that the organism was a significant isolate, but its progression from CA-ASB to CA-UTI still remains a point of discussion and further study. The probable pathogenesis behind this unusual presentation can be explained by the process of formation of biofilms on the surfaces of indwelling catheters. Additionally, the urease producing property of this pathogen helps it to survive and grow in these conditions, causing clinically apparent infection. In a correspondence to the editor, by Wang TK et al., the patient had *P. rettgeri* peritonitis, attributable to the indwelling Tenckhoff catheter, allowing the growth of biofilms [13]. The biofilm production by the bacteria on the surface of the indwelling catheter can be the plausible explanation for the asymptomatic bacteriuria in our patient, apart from the inherent urease producing property of *Providencia* itself. CA-ASB forms a

large reservoir of pathogens, which are resistant to antimicrobials, in the long term care conveniences and tertiary hospitals. The patient-to-patient transmission may occur via urinary catheter or other invasive devices, thus becoming an obvious target for antibiotic therapy, which explains the resistance in such centers and setups [12].

CONCLUSION

Providencia is an emerging nosocomial pathogen which shows a rising trend in resistance with respect to routinely administered antimicrobials. The judicious use of antibiotics, early de-catheterisation and implementation of contact isolation procedures coupled with use of sterile gloves will reduce the risk of patient exposure to this pathogen. This case report has highlighted the importance and rarity of the organism in question, necessitating early identification, treatment and a more comprehensive study of the same. This report may represent a sentinel case that indicates the presence of an antibiotic resistant, human colonising strain of *P. rettgeri* circulating in South India warranting large scale studies of the same.

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