Case Report

Stenotrophomonas maltophilia: Complicating treatment of ESBL UTI

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Abstract

Stenotrophomonas maltophilia (*S. maltophilia*) is a gram-negative bacillus emerging as an opportunistic, nosocomial pathogen associated with a high mortality rate. The organism has been shown to survive several biocides used in the hospital setting. Hospital water sources can serve as a reservoir for *S. maltophilia.* The transmission of *S. maltophilia* to susceptible individuals may occur through direct contact with the source or through the hands of health care personnel. *S. maltophilia* is usually resistant to third-generation cephalosporins, aminoglycosides and antipseudomonal penicillins. These microorganisms are intrinsically resistant to carbapenems, and exposure to these agents has been linked to selection of *S. maltophilia*. There have also been reports of the organism developing resistance to trimethoprim–sulfamethoxazole (TMP–SMX), which was initially considered as the drug of choice for *S. maltophillia* infections. We describe a case of nosocomial urinary tract infection (UTI) due to *S. maltophilia* in a diabetic patient, which the patient developed during treatment with meropenem for UTI due to *Klebsiella pneumonia* that was resistant to TMP–SMX.

Key Words: Antimicrobial sensitivity, *Stenotrophomonas maltophilia*, urinary tract infection

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Received: 20.01.2013, **Accepted:** 18.03.2014

INTRODUCTION

Stenotrophomonas maltophilia (*S. maltophilia*) is a gram negative bacillus emerging as an opportunistic, nosocomial pathogen associated with a high mortality rate.[1,2] Ultramicrocells (UMC) of *S. maltophilia* are able to pass through a 0.2-μm filter. Tap water can harbor opportunistic pathogens at levels that are significant for immunocompromised individuals. Municipal tap water can contain 10^7 bacteria/L, depending upon how frequently the water source is used and the temperature of the water. Hospital water sources can serve as reservoirs of nosocomial pathogens such as *S. maltophilia*. Showerheads equipped with 0.2-μm filters may select for UMC that pass through the filter and form biofilms on the showerhead filter surface, where they can act as a source of infection.[1]

Access this article online	
Quick Response Code:	Website: www.advbiores.net
	DOI: 10.4103/2277-9175.151241

The transmission of *S. maltophilia* to susceptible individuals may occur through direct contact with the source or through the hands of health care personnel. *S. maltophilia* clinical isolates have a higher rate of mutation than environmental isolates, suggesting that clinical isolates adapt to their local environment, e.g. within different areas of the lungs of cystic fibrosis patients.

How to cite this article: Kumar S, Bandyopadhyay M, Chatterjee M, Banerjee P, Poddar S, Banerjee D. *Stenotrophomonas maltophilia*: Complicating treatment of ESBL UTI. Adv Biomed Res 2015;4:36.

It was proposed that antibiotic resistance gene acquisition by *S. maltophilia* strains occurs in the environment, and, upon gaining access to the clinical setting, the strains retain the gene (s). These observations emphasize the need to continue the current monitoring of reported cases of *S. maltophilia*, the emergence and spread of antibiotic resistance and the identification of *S. maltophilia* isolates from sources within and outside the hospital setting.[1] The risk factors for *S. maltophilia* infection have been reported to be: Intensive care unit (ICU) admission, mechanical ventilation, immune deficiency, malignancy, cystic fibrosis, neutropenia, presence of central venous catheters, prolonged hospitalization, previous therapy with broad-spectrum antibiotics and debilitation.[1,2]

S. maltophilia is usually resistant to third-generation cephalosporins, aminoglycosides and antipseudomonal penicillins.[1,3] These microorganisms are intrinsically resistant to carbapenems, and exposure to these agents has been linked to the selection of *S. maltophilia*.[1-4] Resistance can also emerge during therapy.[5] Recently, these infections are being documented in patients without traditional risk factors. The spectrum of infection includes bacteremia, catheter-related infection, pneumonia, ophthalmic infections, complicated biliary and urinary tract infection (UTI) and skin and soft tissue infection.[3,6]

Trimethoprim-sulfamethoxazole (TMP-SMX) is the therapeutic agent of choice, but resistance is increasingly being reported. Susceptibility to alternative agents is unpredictable. Using the checkerboard method, some synergism has been observed between tigecycline and TMP-SMX, and between tigecycline and amikacin, against *S. maltophilia*. *In vitro* pharmacodynamic model results revealed that TMP-SMX in combination with either ciprofloxacin, ceftazidime or tobramycin demonstrated higher bactericidal efficacy against *S. maltophilia* clinical isolates than TMP-SMX alone.[1] Combination therapy and alternative routes of drug administration, such as aerosolized aminoglycoside, might be necessary.[3,6] In addition to antimicrobial chemotherapy in the management of *S. maltophilia* infection, several investigators have stressed the importance of removing infected vascular access devices or prosthetic material. We present a case of *S. maltophilia* UTI in a diabetic patient, which developed as a complication of treatment of nosocomial UTI due to *Klebsiella pneumoniae*. The isolate was resistant to cotrimoxazole and was successfully treated with piperacillin + tazobactam.

CASE REPORT

A 63-year-old male patient was admitted with a history of altered sensorium for the last 3 days. The patient was a known diabetic, diagnosed 20 years back. The patient had undergone a below-knee amputation for diabetic foot 4 months back. On admission, the patient was stupurous and on general examination, the patient had pallor and was afebrile. The blood investigations showed that the patient was hypoglycemic, with a capillary blood glucose level of 12 mg/dL. He was treated conservatively and the blood sugar became stable at about 110-135 mg/dL.

On the third day of his hospital stay, the patient became febrile. The urine sent for routine examination showed plenty of pus cells and the urine culture showed significant growth of Klebsiella spp. ($>10^5$ colony forming units/milliliter). The isolate was found to be sensitive by the Kirby Bauer Disc Diffusion technique (KBDD) to colistin, meropenem, cefoperazone + sulbactam, doxycycline and tigecycline and was resistant to nalidixic acid, nitrofurantoin, amikacin, cefotaxime, cefepime, cefoperazone and piperacillin + tazobactam. The isolate was found to be an extended-spectrum β-lacatamase (ESBL) producer as per the CLSI guidelines.[7] The blood parameters were as follows: Total leukocyte count was 24,100/mm^3, with 88% neutrophils, 8% lymphocytes, 3% eosinophils and 1% basophils, hemoglobin − 8.4 gm% and platelet count − 424,000/mm^3. The biochemical parameters were as follows: Serum sodium 137 meq/L, serum potassium 3.5 meq/L, urea 33 mg/dL, creatinine 0.87 unit/L and blood sugar 119 mg/dL. Ultrasonography of the abdomen showed urinary bladder wall thickening, with sludge noted in the urinary bladder. The patient was started on intravenous meropenem, following which he showed marked improvement and become afebrile. The blood cultures of the patient showed no growth. The repeated blood counts showed improvement, but the patient developed serum electrolyte imbalance (Na^+ - 123 meq/L, K^+ - 3.9 meq/L, Cl^- − 8.9 meq/L). The urine culture performed on the sixth day of admission showed no growth.

After 8 days of afebrile period, during which the patient was being treated for electrolyte imbalance, he started developing fever of a low grade. On this occasion, the urine examination revealed pus cells 5-6/high power field (hpf) and red blood cells 6-7/hpf. The urine cultures showed growth of nonlactose-fermenting colonies with significant colony count ($>10^5$ cfu/mL). The isolate was catalase positive, oxidase negative, motile, gram negative rods, which reduced nitrates; oxidized glucose, lactose, mannitol and maltose; hydrolyzed gelatin; and was lysine decarboxylase test positive

and arginine hydrolysis negative. The organism was identified as *Stenotrophomonas maltophilia*, identified by standard laboratory procedures and confirmed with API 20 NE test strips (Bio-Me´rieux, Marcy l'Etoile, France). The isolate was found to be susceptible to polmyxin B, cefoperazone, gatifloxacin, piperacillin + tazobactam, levofoxacin and colistin and was resistant to doxycycline, cotrimoxazole, meropenem, amoxicillin + clavulanic acid, cefotaxime, ceftazidime, ticaricillin + clvulanic acid, nalidixic acid and amikacin by the disc diffusion method as per the CLSI guidelines.[7]

The repeated urine cultures showed the growth of the same organism with significant colony count and similar antibiogram. The blood cultures sent were found to be sterile all along. The patient was started on piperacillin + tazobactam, to which the patient responded with clearance of the pyuria and repeated urine cultures showing no growth. The patient was later discharged, at the time of which he was doing well.

DISCUSSION

S. maltophilia has become an important nosocomial pathogen in debilitated patients. Previous guidelines did not advocate treatment for every patient with a positive *S. maltophilia* culture. The inability/difficulty to distinguish between colonization and infection had fostered the belief that *S. maltophilia* is of limited pathogenicity. However, *S. maltophilia* should not be routinely dismissed as a colonizer, like in the case of our patient, in which the symptomatic patient showed significant colony count on repeated cultures. It is imperative to identify patients at high risk for mortality early in the course of illness. Thus, the identification of various predictors of mortality in these patients serves as an important tool to guide clinicians toward the evaluation of a risk-to-benefit ratio in initiating therapy for *S. maltophilia* infections.[1,3]

Two inducible β-lactamases, a zinc-containing penicillinase (L1) and a cephalosporinase (L2), are responsible for the high proportion of resistance to β-lactams. The presence of an aminoglycoside acetyl-transferase accounts for the resistance to aminoglycosides. Furthermore, many isolates possess efflux pumps, which are the main determinants of quinolone resistance. Other mechanisms of resistance to quinolones may emerge through spontaneous mutations in the outer membrane proteins.[3,6] TMP-SMX is the antibiotic of choice for the treatment of *S. maltophilia* infections,[2,4] but the isolate in our study was found to be resistant to the same.

Studies have shown that *S. maltophilia* biofilms demonstrated tolerance to the biocides like bleach, triclosan and sodium dodecyl sulfate (SDS). *S. maltophilia* has been recovered from a contaminated deionized-water-diluted hospital antiseptic solution and from contact lens preservative solutions. The *qacEΔ1*gene, encoding tolerance to antiseptics containing quaternary ammonium compounds, has also been detected in *S. maltophilia* clinical isolates. These observations of metal resistance in environmental isolates suggest that similar to the acquisition of antimicrobial drug resistance, the acquisition of metal resistance occurs in the natural environment. Environmental isolates of *S. maltophilia* found in the clinical/medical setting may simply be maintaining metal resistance genes when challenged with antimicrobials containing metals. These results emphasize the importance of maintaining good hygiene practices when handling antiseptics and preservative solutions.[1]

Therapy for infections with these pathogens is challenging because of their resistance to most antimicrobial agents and the variable antimicrobial susceptibility of different strains. These microorganisms are intrinsically resistant to carbapenems, and exposure to these agents has been linked to selection of *S. maltophilia*, like in the case of our patient who developed UTI due to *S. maltophilia* while he was on therapy for ESBL-producing Klebsiella species infection. As an alternative to the use of antibiotics, essential oils from plants like cinnamon, thyme and clove demonstrated the highest level of antimicrobial activity and inhibited all tested strains of *S. maltophilia*. Future research is needed to elucidate the precise chemical composition of the oil that determines the mechanism of action (bactericidal/bacteriostatic activity) of these oils.[1]

The use of phage therapy may be an alternative to the use of antibiotics to treat *S. maltophilia* infections. Phage therapy is not used in ordinary clinical practice for the treatment of *S. maltophilia* infections. *S. maltophilia* phages have been isolated from sputum samples, pleural effusions and catheter tips. Research is needed to determine whether phage-coated catheters demonstrate significantly reduced numbers of viable cells when the catheters are exposed to *S. maltophilia*, whether the *S. maltophilia* biofilms can be reduced or removed and whether *S. maltophilia* develops resistance to the phage. Together, the observations from the studies suggest that it is possible that a cocktail of surfactant, antimicrobial peptides and phage may provide a suitable alternative to the administration of antibiotics.[1]

A major challenge facing clinical personnel will be to hinder *S. maltophilia*'s ability to adapt to the local environment of the patient and to alter antimicrobial strategies to keep pace with the evolution of *S. maltophilia*. The development of new treatments needs to take a microbial ecology/community approach to consider the interaction of *S. maltophilia* with host cell surfaces. The use of biocides in clinical/medical settings should be carefully controlled to avoid encouraging the spread of biocide-tolerant *S. maltophilia* strains (e.g. those carrying the *qac* gene cassette). To combat the increasing incidence of *S. maltophilia* infections in hospitals and clinics, education to increase awareness of health care personnel is a key step in preventing the transmission and spread of this opportunistic pathogen. The prevention of biofilm formation and a reduction of the risk of infection within the clinical setting necessitate an observation of aqueous-associated environments and regular cleaning and disinfection regimens for surfaces of medical equipment that comes into contact, directly or indirectly, with patients. The hygienic practice of hand washing by health care personnel must continually be reinforced to reduce the possibility of organism transfer from tap water to patients. The avoidance of the use of hospital tap water for bathing and cleaning of wounds is a necessary measure of care for particularly vulnerable populations. The discarding of residual antibiotic solutions, residual and possibly contaminated hand soap solutions and patient body fluids into the hospital plumbing system should be avoided. An increased vigilance for the observation and replacement of worn parts of susceptible surfaces, such as old deteriorating plumbing systems, can help reduce the risk of infection. Steps taken such as these are actions that can help lower the number of fatalities associated with *S. maltophilia* infections.

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Source of Support: Nil, **Conflict of Interest:** None declared.