A rare case of *Stenotrophomonas maltophilia* resistant to Trimethoprim-Sulfamethoxazole (co-trimoxazole)

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ABSTRACT

Stenotrophomonas maltophilia (*S. maltophilia*) is becoming increasingly recognised as an important nosocomial pathogen. Treatment of invasive *S. maltophilia* infections is difficult due to its intrinsic or acquired resistance to different antibiotics. Trimethoprim-sulfamethoxazole (co-trimoxazole) sensitivity is used as an identification test for *S*. *maltophilia* and is recommended as the agent of choice for treatment. But resistance to co-trimoxazole is a serious threat. This report describes the first isolation of *S. maltophilia* resistant to co-trimoxazole from a patient treated at RIPAS Hospital, Brunei Darussalam.

Keywords: Nosocomial infection, anti-microbial resistance, infections, *Xanthomonas maltophilia*

INTRODUCTION

Stenotrophomonas maltophilia (*S. maltophilia*), formerly known as *Pseudomonas* or *Xanthomonas maltophilia*, is a Gram-negative aerobic, non-lactose fermentative bacillus, frequently isolated from water, soil, animals, and plant materials and environment as well as hospital equipment. *S. maltophilia* is generally considered to be an opportunistic pathogen, mainly causing nosocomial infection although community – acquired infections too have been reported. [1-3]

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The most frequent clinical manifestation of *S. maltophilia* infection is pneumonia. However, the majority of *S. maltophilia* isolates when recovered from clinical specimens are considered as colonisation rather than infections. *S. maltophilia* infection is more likely to occur in patients admitted to the intensive care unit, on mechanical ventilation or tracheostomy, with advanced age or with malignancy, patients with higher Acute Physiology And Chronic Health Evaluation 2 (APACHE-2) score and specially among patients who are exposure to broad–spectrum antimicrobial agents, such as carbapenems, extended–spectrum cephalosporin and fluoroquinolones. [1, 4, 5] This organism is intrinsically resistant to

carbapenems and exposure to these agents may perpetuate overgrowth and facilitate subsequent super infection [6] due to eradication of the normal flora by these broad spectrum antibiotics. Nosocomial *S. maltophilia* pneumonia is associated with high mortality, particularly when associated with bacteraemia and airway obstruction. This could be further complicated by septic shock and multiple organ dysfunctions. The second commonest infection caused by S. *maltophilia* is central venous catheter related bacteraemia. [1] It is also commonly isolated from patients with cystic fibrosis. [5] Other less common infections are endocarditis, meningitis, ocular urinary tract, skin and soft tissue infections. [1, 5]

Treatment of invasive *S. maltophilia* infections is difficult because of its high intrinsic or acquired resistance to various classes of antibiotics. [1, 7] Until recently *S. maltophilia* was universally sensitive to co-trimoxazole, thus it was not only used as one of the method to identify this organism in microbiological laboratory but also recommended as the agent of choice for treatment for those patient infected with *S. maltophilia*. However, the development of resistance to this antibiotic represents a real challenge. Sporadic cases of resistance to co-trimoxazole have been reported in various parts of the world. We report a case of *S. maltophilia* resistant to co-trimoxazole.

CASE REPORT

A 59–year-old man with hypertension, diabetes mellitus, chronic heart failure and dyslipidaemia, was admitted to the Intensive Care Unit (ITU) 35 days following a coronary artery bypass graft (CABG) surgery, with acute abdomen due to perforated bowel and peritonitis, leading to sepsis and multi-organ failure. Complications following CABG surgery necessitated prolonged ventilator support; hence tracheostomy was performed on 7th post-operative day. During post-operative period he developed jaundice, encephalopathy and was transferred with acute abdomen suspected of paralytic ileus suggested by a computed tomography (CT) scan.

He was treated with on and off with intravenous (IV) broad spectrum antibiotics namely meropenem and ceftazidime following surgery. On admission he was afebrile, but was hypotensive (90/60 mmHg), tachycardia (100/min) and had a high white cell count (WBC) (25×10^9/L, normal 4-11.0). Chest radiography showed patchy broncho-pneumonia and mild pleural effusion and he was commenced on IV meropenem (500mg 8hourly) and amoxicillin-clavulanic acid (1.2g IV 12th hourly). Surgery for perforated bowel was withheld due to haemodynamic instability. Unfortunately, his condition continued to deteriorate and he died two days following admission to the ICU.

Tracheal aspirate sent on the day of admission isolated a Gram negative, non-lactose fermenting, oxidase negative bacilli which was identified by API 20E (ANALYTICAL PROFILE INDEX) ® (bioMerieux) as *S. maltophilia* and it was found to be resistant to co-trimoxazole with no-zone of inhibition by antimicrobial susceptibility testing done according to modified Kirby Bauer's disc diffusion method following the guidelines published by Clinical Laboratory Standard Institute 2012 (CLSI 2012). [8] Since this isolate showed uncommon sensitivity pattern by being resistant to co-trimoxazole, both identity and sensitivity were

confirmed by repeating the conventional methods and also by VITEK 2® (bioMerieux) automated system for identification and antibiotic sensitivity. By these methods the isolate was confirmed as co-trimoxazole resistant *S. maltophilia*. Resistance of this isolate to co-trimoxazole was further confirmed by VITEK 2® (BioMerieux) method showing Minimum Inhibitory Concentration (MIC) value for co-trimoxazole against this *S. maltophilia* isolate as >8/312 (sensitive range ≤2/38 and resistant range ≥4/76) confirming the resistance to co-trimoxazole demonstrated by Kirby Bauer's method. This isolate was resistant to all other antibiotics tested other than levofloxacin.

DISCUSSION

S. maltophilia is a highly resistant, ubiquitous environmental bacterium causes infections that result in increased morbidity and mortality especially in patients with impaired immune system. *S. maltophilia* is known to have intrinsic resistance against various antibiotics. Various molecular mechanisms including plasmids, integrons, and transposons of *S. maltophilia* contribute to its multiantibiotic resistance. [9-11] For decades co-trimoxazole has been considered as the drug of choice for the treatment of *S. maltophilia* infections. [9, 11] But appearance of resistance to co-trimoxazole is posing a serious threat to infections caused by this organism. This resistance is mediated through class 1 integrons and IS*CR* elements linked to *sul*2 genes in *S. maltophilia.* [9-11] Rates of resistance to co-trimoxazole ranged from 2% in Canada and Latin America to 10% in Europe. [7, 9, 10] Alternative agents such as ticarcillin–clavulanate, ceftazidime, flouroquinolones, minocycline and chloramphenicol have been used with variable success and most often as combination regimens. [7, 13] The newer fluoroquinolones appear to be more active than older agents [7], but still co-trimoxazole or ticarcillin–clavulanic acid is considered to be the first choice for clinical treatment. [1] The addition of another antimicrobial agent such as ticarcillin–clavulanic acid, fluoroquinolones or ceftazidime to co-trimoxazole should be considered if there is a significant incidence of resistance to co-trimoxazole in the healthcare institution especially in neutropenic and severely ill patients. [7, 11, 14]

To our knowledge, this is the first report of isolation of *S. maltophilia* resistant to co-trimoxazole from Brunei Darussalam. Prolonged mechanical support, exposure to broad spectrum agents and impaired host defences could have been the predisposing factors for *S. maltophilia* infection in this patient. Further ISCR elements linked to sul2 genes which are known to be carried in Enterobacteriacae could have been transposed to *Stenotrophomonas maltophilia* to confer its resistance to co-trimoxazole. [9] Finding of this co-trimoxazole resistant isolate in Brunei Darussalam with sporadic reporting of this organism from wider geographical regions [7, 9], reinforce the need for on-going resistance surveillance internationally and nationally.

Steps should be taken to prevent *S. maltophilia* infection in general, and also specifically to prevent spread of this resistant strain. Hence proper antibiotic stewardship including avoidance of inappropriate use of antibiotics namely broad spectrum antibiotics, avoidance of prolonged use of foreign devices, reinforcement of hand hygiene practices and application of appropriate infection

control practices would be necessary to prevent the spread of infection by this organism.

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