

Received: 2019.11.17

Accepted: 2020.03.24

Available online: 2020.05.21

Published: 2020.05.25

Stenotrophomonas maltophilia: An Emerging Pathogen of the Respiratory Tract

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Female, 70-year-old
Final Diagnosis: *Stenotrophomonas maltophilia*
Symptoms: Difficult to breath, patient could not wean from oxygen/premature
Medication: —
Clinical Procedure: —
Specialty: General and Internal Medicine

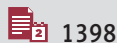
Objective: Rare disease
Background: *Stenotrophomonas maltophilia* has the propensity to cause a plethora of opportunistic infections in humans owing to biofilm formation and antibiotic resistance. It is often seen as a co-organism along with *Pseudomonas aeruginosa*.

Case Report: A 70-year-old woman with several co-morbidities presented reporting hypoglycemia and dyspnea. An imaging study of the chest was suggestive of deterioration of pneumonia, with increased opacities. Initial respiratory cultures were negative, while subsequent repeat cultures revealed the growth of *Stenotrophomonas maltophilia* susceptible to trimethoprim plus sulfamethoxazole and levofloxacin. The patient had a poor prognosis and eventually died despite appropriate measures.

Conclusions: A decline in the clinical status of a patient such as ours makes it hard to quickly diagnose this organism correctly. Physicians should thus be cautious of *Stenotrophomonas maltophilia*-induced infection and more emphasis should be placed on appropriate treatment due to the emerging risk of antibiotic resistance.

MeSH Keywords: Antibiotic Prophylaxis • Pneumonia • *Stenotrophomonas maltophilia* • Urinary Catheterization

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/921466>



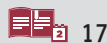
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Background

Stenotrophomonas maltophilia (*S. maltophilia*), formerly known as *Pseudomonas maltophilia* and *Xanthomonas maltophilia*, is an anaerobic, gram-negative, non-fermentative bacillus. It is an ubiquitous organism that has been isolated from humans, animals, soil, and food [1]. It is the only species of the genus *Stenotrophomonas* that is known to cause infection in humans, especially in immunocompromised patients and patients with medical devices like indwelling catheters (e.g., intravenous lines, mechanical ventilators, catheters, and feeding tubes). It is an organism with a low virulence factor and therefore can cause several cross-infections, in addition to opportunistic infections [2].

Although *S. maltophilia* rarely causes community-acquired infections, there has been an emerging trend of nosocomial infections, especially in patients with chronic underlying illnesses. The prevalence of *S. maltophilia* infection has increased from 0.8–1.4% during the years 1997 to 2003, to 1.3–1.68% from 2007 to 2012 [3].

The organism has also been reported to cause urinary tract infection [4], mucocutaneous and soft tissue infections [5], bacteremia [6], pneumonia [2], endocarditis [7], osteomyelitis [8], and meningitis [9]. Outbreaks and pseudo-outbreaks of *S. maltophilia* have also been reported to occur due to endoscopic procedures, especially bronchoscopy [10].

S. maltophilia-associated morbidity and mortality can be due to various factors such as innate resistance and extensive antibiotic treatment, adding to the antibiotic resistance and the underlying co-morbid conditions in patients. For all these reasons, the present case report focuses on the clinical significance of *S. maltophilia* in respiratory infections. Here, we discuss the case of a 70-year-old woman with respiratory cultures growing *S. maltophilia*, complicated with sepsis secondary to pneumonia.

Case Report

A 70-year-old woman presented to the Emergency Department from a skilled nursing facility with hypoglycemia and reported shortness of breath for the past 2 days. She had a medical history of a cerebrovascular accident, chronic respiratory failure status following tracheostomy and percutaneous endoscopic gastrostomy, adenocarcinoma of the lung, anemia, hypertension, and chronic obstructive pulmonary disease. She was a current smoker. On arrival, she had a temperature of 33.3°C, pulse of 48 beats per minute, blood pressure of 107/93 mmHg, and oxygen saturation of 90% on room air, requiring 6 L of supplemental oxygen to maintain saturation at



Figure 1. Chest radiograph on admission, showing bilateral coarsened appearance of the pulmonary parenchyma.

100%. Her respiratory rate was 15 breaths/minute and blood glucose level was 122 mg/dl. Physical exam revealed crackles at the right lung base, which was chronic according to her past medical records. On admission, the leukocyte count was 21 K/uL. Lower respiratory cultures done on the day of admission revealed growth of rare gram-positive cocci. The patient had a complicated hospital course with the development of new first-degree atrioventricular block, ischemic stroke, urosepsis, and cardiac arrest contributing to deterioration of her clinical condition. A chest radiograph showed bilateral coarsened appearance of the pulmonary parenchyma (Figure 1).

A computed tomography (CT) scan of the chest that was done on the day of admission revealed bilateral upper and lower lobe infiltrates suggestive of progression of pneumonia along with pleural-based infiltrate in the left lower lung. Empiric antibiotic treatment with vancomycin and cefepime were initiated on the day of admission. Urine culture revealed growth of *Proteus mirabilis*, which was sensitive to cefepime. The leukocyte count peaked at 71 K/uL during the hospital course. Repeat respiratory cultures performed 2 weeks later revealed growth of *S. maltophilia* (cultures are not obtained by bronchoscopy). Sensitivity tests for minimum inhibitory concentration and Kirby-Bauer susceptibility tests revealed sensitivity to trimethoprim plus sulfamethoxazole (TMP-SMX) and levofloxacin and resistance to ceftazidime (Table 1).

The patient was subsequently started on intravenous levofloxacin 750 mg every 48 hours (renally dosed), for a total of 10 days, because she was expected to have a slow recovery given her overall clinical status. A repeat chest x-ray showed worsened diffuse bilateral mixed interstitial and airspace opacities (Figure 2). A repeat CT of the chest with contrast was done after

Table 1. Susceptibility of *S. maltophilia* with minimum inhibitory concentration.

	MIC (<i>S. maltophilia</i>)	Susceptibility
Ceftazidime	>16	R
Levofloxacin	<2	S
Trimethoprim+ sulfamethoxazole	<2/38	S

MIC – minimum inhibitory concentration; R – resistant; S – susceptible.

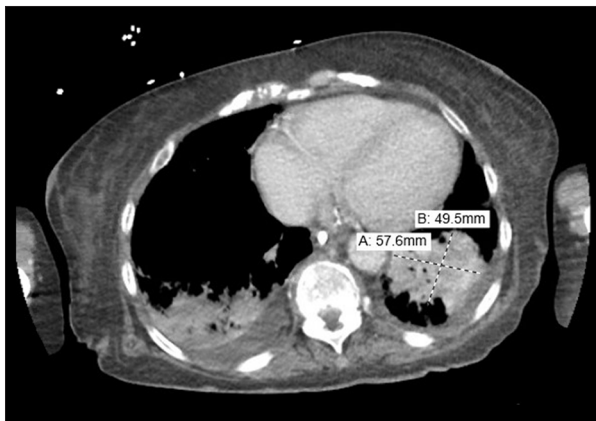


Figure 2. CT chest showing irregularly marginated 5.7×4.9 cm pleural-based infiltrate.

10 days, revealing new right upper lobe infiltrates. Another CT chest done after 2 days showed further progression of consolidation. A repeat CT chest done after 3 weeks revealed progressive bilateral consolidation of the lungs. Due to worsening clinical status, vancomycin, cefepime, and metronidazole were added, which was later narrowed down to meropenem given her negative MRSA result. Despite the rigorous management, the patient died due to cardiac arrest caused by the multiple co-morbid conditions and also probably due to a delay in the diagnosis of *S. maltophilia* pneumonia.

Discussion

S. maltophilia possesses various characteristics that contribute to its pathogenicity. Biofilm formation is one of the major reasons for development of antibiotic resistance [11]. The presence of flagella and fimbriae further contribute to biofilm formation [12]. Another factor responsible for the virulence of *S. maltophilia* is the outer membrane lipopolysaccharide which results in colonization [11]. *S. maltophilia*-induced airway inflammation is likely due to stimulation of monocytes and alveolar macrophages by the lipid A present in the lipopolysaccharide. This results in the release of tumor necrosis factor α

and subsequent inflammation. It also has the ability to form variants of small colonies, which has been reported to be one of the reasons for its persistence in chronic infections. Such variants are not easily detected in clinical specimens. It is not uncommon to diagnose the infection with the organism late in the course, as symptoms are usually overshadowed by the poor clinical condition of patients. Thus, clinical deterioration despite adequate treatment may demand the clinician to suspect infection with *S. maltophilia*, as symptoms are usually non-specific and mimic other common pathogens causing sepsis.

S. maltophilia infection is more commonly seen in neutropenic and immunosuppressed patients [13]. Our patient had a history of lung carcinoma and chronic obstructive pulmonary disease and was using a tracheostomy collar on a long-term basis.

The detection of *S. maltophilia* can be challenging. However, recent studies have revealed that matrix-assisted laser desorption/ionization time-of-flight mass-spectrometry (MALDI-TOF MS) is highly accurate, less expensive, and helps in quick microbial taxonomic identification. Thus, the current methods of detection can be substituted with MALDI-TOF MS for better efficiency [14].

According to the World Health Organization (WHO), *S. maltophilia* is considered one of the predominant organisms in hospitals causing pneumonia and bacteremia, usually resistant to most antibiotics and with the ability to rapidly change its multi-resistant phenotype [15]. The increase in antibiotic resistance has been attributed to the development of various mechanisms allowing pathogens to thrive, such as the presence of acquired resistance genes, reduced permeability of outer membranes, chromosomal and plasmid-encoded transposons, and efflux pumps. Beta-lactam resistance occurs due to inducible beta-lactamases, a zinc-containing penicillinase (L1) and a cephalosporinase (L2). Penicillin-binding proteins (PBPs) are responsible for the biosynthesis of peptidoglycans, and a putative PBP1a gene was recently reported to cause basal-level L1/L2 β -lactamase hyper production in *S. maltophilia* [11].

Management can be affected if there is inability to differentiate *S. maltophilia* infection from *S. maltophilia* colonization [16]. Treatment is burdensome, especially due to difficulty in early diagnosis and initiation of pathogen-directed treatment. However, once the pathogen is suspected, the treatment of choice for both empiric and directed therapy is trimethoprim-sulfamethoxazole (TMP-SMX) [3]. In those who are immunocompromised, the addition of a second agent such as levofloxacin may also be recommended. Patients who are allergic to TMP-SMX can be alternatively be treated with levofloxacin or ceftazidime. The duration of antibiotic therapy varies from 7 days for pneumonia to up to 14 days for bacteremia. A longer duration of therapy is often recommended for immunocompromised hosts.

However, due to the increasing resistance to antibiotics, especially monotherapy, there has been a rising trend towards use of combination drugs. A study by Betts et al. revealed that combining TMP/SMX or β -lactam/ β -lactam inhibitors with rifampin resulted in better outcomes [17].

Conclusions

It is prudent to maintain a high index of suspicion for atypical and resistant organisms such as *S. maltophilia* infection, especially in patients with co-morbidities and not responding to empiric treatment with broad-spectrum antibiotics. Clinical decision-making should be prompt and tailored according to the

antimicrobial susceptibility, since delay in treatment is an important risk factor for bacteremia and sepsis due to *S. maltophilia*. We believe our patient developed sepsis and subsequent cardiac arrest due to *S. maltophilia* in addition to her immunosuppressed state and co-morbid conditions. Prevention of the continued rise in rates of infection can be encouraged by continued enforcement of use of sterile medical techniques, the utilization of lines and catheters for appropriate indications and durations, and practicing good microbial stewardship when prescribing antibiotics.

Conflict of interest

None.

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