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Suitable empiric antibiotic therapy saves lives in nosocomial pneumonia caused by *Stenotrophomonas maltophilia*

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Aim: *Stenotrophomonas maltophilia* is a nosocomial pathogen of increasing importance. Empiric antibiotic therapy for *S. maltophilia* infection is difficult because the microorganism is resistant to a number of agents typically used for health care associated infections, thus potentially increasing mortality. This study investigates 23 nosocomial pneumonia cases caused by *S. maltophilia*, the antibacterial sensitivity of the bacterium and the effect on mortality of suitable empiric therapy.

Materials and methods: Twenty-three patients with nosocomial pneumonia caused by *S. maltophilia* between January 2000 and December 2006 at the Karadeniz Technical University Hospital were retrospectively investigated.

Results: Suitable empiric therapy was used with 12 patients (52.2%), but the therapies administered to the other 11 patients were inappropriate for *S. maltophilia* infection. Eight (72.7%) of the patients who were not given suitable empiric antibiotherapy died (P = 0.002).

Conclusion: The appropriate empiric antibiotic was administered to only 12 of the patients. The mortality rate among those patients to whom appropriate empiric antibiotics were not administered was high, proving that suitable empiric therapy is vitally important. Due to the increase in mortality, it is essential to initiate appropriate empiric therapy by carefully evaluating the risk factors for *S. maltophilia* in nosocomial pneumonia and taking sputum and bronchoalveolar lavage specimens without delay.

Key words: *Stenotrophomonas maltophilia*, nosocomial pneumonia, empiric antibiotic

S. maltophilia'nın neden olduğu hastane kaynaklı pnömonide uygun ampirik antibiyotik tedavisi yaşam kurtarır

Amaç: *Stenotrophomonas maltophilia* önemi giderek artan bir hastane patojenidir. *S. maltophilia* infeksiyonunda ampirik antibiyotik tedavisi zordur. Bu mikroorganizma sağlık bakımı ile ilişkili infeksiyonlarda kullanılan çok sayıda ajana dirençlidir ve bu nedenle de mortalite artmaktadır.

Bu çalışma *S. maltophilia*'nın neden olduğu 23 hastane kaynaklı pnömoni vakasını, bakterinin antibakteriyel duyarlılığını ve uygun ampirik tedavinin mortalite üzerine etkisini incelemektedir.

Yöntem ve gereç: Karadeniz Teknik Üniversitesi Hastanesinde Ocak 2000 ve Aralık 2006 tarihleri arasında *S. maltophilia*'nın neden olduğu 23 hastane kaynaklı pnömoni hastası retrospektif olarak değerlendirildi.

Bulgular: Uygun ampirik tedavi 12 (% 52,2) hastaya uygulandı. Diğer 11 hasta için uygulanan tedavi *S. maltophilia* infeksiyonu için uygun değildi. Uygun ampirik antibiyoterapi almayan hastaların sekizi (% 72,7) öldü (P = 0,002).

Sonuç: Uygun ampirik antibiyotik yalnız 12 hastaya uygulandı. Uygun ampirik antibiyotik uygulanmayan bu hastalar arasında mortalite oranı yüksekti. Bu da uygun ampirik tedavinin hayati önemli olduğunun kanıtıdır. Mortalitedeki yükseklik nedeniyle hastane kaynaklı pnömonide balgam ve bronkoalveolar lavaj örneği gecikme olmaksızın alınarak ve *S. maltophilia* için risk faktörleri dikkatlice değerlendirilerek uygun ampirik tedavinin başlanması gereklidir.

Anahtar sözcükler: *Stenotrophomonas maltophilia*, hastane kaynaklı pnömoni, ampirik antibiyotik

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Introduction

Nosocomial pneumonia is the leading cause of mortality attributed to health care associated infections (1). *Stenotrophomonas maltophilia*, which is a cause of nosocomial pneumonia, is a nosocomial pathogen of increasing importance (2-4). This bacterium is a non-fermentative, aerobic, and gram-negative bacillus. The risk factors for *S. maltophilia* infection include neutropenic and hematological malignancy, the use of broad spectrum antibiotics, immunosuppression, especially due to chemotherapy, prolonged hospitalization, and intravenous catheter use (2,3,5). Empiric antibiotic therapy for *S. maltophilia* infection is difficult because the organism is resistant to a number of agents typically used for health care associated infections, thus potentially increasing mortality (6).

This study examines 23 nosocomial pneumonia cases caused by *S. maltophilia*, together with the risk factors and antibacterial sensitivity of this bacterium, and discusses the effect of suitable empiric therapy on mortality.

Materials and methods

Twenty-three patients with nosocomial pneumonia caused by *S. maltophilia* and treated between January 2000 and December 2006 at the Karadeniz Technical University Hospital were retrospectively investigated. Nosocomial pneumonia is defined as new lung infiltrates plus evidence that the infiltrates are of infectious origin, such as fever, leukocytosis or purulent sputum occurring in patients hospitalized for at least 48 h (7). *S. maltophilia* was identified in quantitative bronchoalveolar lavage (BAL), sputum or endotracheal-aspiration culture, or blood culture. Identification of the causative microorganisms and antibiotic sensitivity tests were performed using the automated Sceptor panel (Sceptor system, Becton Dickinson, USA), disk diffusion test. Each patient's demographic data were recorded for assessment of potential risk factors for *S. maltophilia* pneumonia: age, sex, presence of predisposing underlying diseases, length of hospitalization, and previous antibiotic use or immunosuppressive therapy.

Statistical Analysis

Data obtained by measurement are given as mean ± standard deviation. Data obtained by counting are given as numbers (%); analyses were performed using the chi-square test. $P < 0.05$ was taken as statistically significant.

Results

Twenty-three patients with *S. maltophilia* pneumonia were investigated. The clinical characteristics of the patients are summarized in Table 1. The mean age of the patients, 6 female and 17 male, was 52.7 ± 18.7 years. Four had lung cancer, 2 had lymphoma, 2 others had had leukemia, and 8 had chronic pulmonary disease. Eleven patients received immunosuppressive therapy, and 3 had neutropenia. All the patients had used antibiotics before contracting nosocomial pneumonia. Mean length of hospitalization was 36.7 ± 31.4 days. Suitable empiric therapy was administered to 12 patients (52.2%), but the therapies administered to the other 11 patients were not appropriate for *S. maltophilia* infection. Nine (39.1%) patients with *S. maltophilia* pneumonia died. Eight (72.7%) of the patients who did not receive suitable empiric antibiotherapy died ($P = 0.002$). Trimethoprim-sulfamethoxazole was administered to 1 patient alone because *S. maltophilia* had been isolated just 1 day before he died, while in the other patients identification was possible only after their deaths. When we investigated the reason for delay of the culture results, we concluded that the sputum and BAL samples from the patients had been taken behind schedule, meaning that suitable antibiotic therapy was not initiated.

As shown in Table 2, most *S. maltophilia* isolates were resistant to Ticarcillin-clavulanate aminoglycosides, ciprofloxacin and betalactam antibiotics, and trimethoprim-sulfamethoxazole were the most active agents for *S. maltophilia* strains.

Discussion

Whether *S. maltophilia*, widely available in many natural environments such as water, soil, and vegetable and animal sources, is a cause of infection was long a matter for discussion. However, it has

Table 1. Patients' clinical characteristics.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11	Case 12	Case 13	Case 14	Case 15	Case 16	Case 17	Case 18	Case 19	Case 20	Case 21	Case 22	Case 23	Mean±SD or %
Age	48	51	40	65	58	71	63	48	32	76	69	17	80	34	57	80	51	65	56	68	34	31	17	52.7±18.7
Sex (F/M)	M	F	M	M	M	M	M	F	M	M	M	M	M	F	M	M	M	F	M	F	F	M	M	6/17
Pneumonia diagnosis																								
-new lung infiltrates	-	-	-	+	+	-	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	-	+	69.6
-purulent sputum	+	+	+	-	-	+	+	+	-	-	+	+	+	+	-	+	+	-	+	-	+	+	+	69.6
-fever	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	-	+	+	+	86.9
-leukocytosis	+	+	-	+	+	-	+	+	-	-	+	-	-	-	+	-	+	+	-	+	+	+	+	60.9
Culture sample																								
-bronchoalveolar lavage	-	-	-	-	+	+	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	17.4
-sputum	+	+	+	-	-	-	+	-	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-	26.1
-blood	-	-	+	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	+	-	17.4
-endotracheal-aspiration	+	-	-	+	-	-	-	+	-	-	+	-	+	+	+	+	+	+	+	+	-	+	+	60.9
Underlying disease																								
-Lung cancer	-	+	-	-	-	+	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	17.4
-Lymphoma	+	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	8.7
-Leukemia	-	-	+	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	8.7
-Chronic pulmonary disease	-	-	-	+	+	-	+	+	-	-	-	-	+	-	+	+	-	-	-	+	-	-	-	34.8
Immunosuppressive therapy	+	+	+	-	-	+	-	-	+	-	+	+	-	-	-	-	+	-	+	+	-	+	-	47.8
Neutropenia	-	-	+	-	-	-	-	-	+	-	-	+	-	-	-	-	-	-	-	-	-	-	-	13.0
Prior antibiotic therapy																								
-Penicillin	+	-	+	-	+	-	+	-	+	+	+	-	-	+	-	-	-	-	-	-	+	-	-	39.1
-Third- or fourth- generation cephalosporin	-	+	-	+	+	+	-	+	+	-	-	+	+	+	+	+	+	-	+	+	+	-	+	69.6
-Imipenem	+	-	-	-	-	+	-	-	-	-	+	+	+	+	+	+	+	+	-	-	+	+	+	56.5
Hospitalization days	45	78	9	53	31	35	36	41	24	38	47	29	15	99	168	35	26	52	20	109	99	89	38	52.9±37.7
Hospitalization days prior to pneumonia	39	44	6	29	8	27	21	23	19	27	18	13	12	81	110	18	11	34	15	103	81	82	24	36.7±31.4
Suitable empirical therapy	-	-	-	+	-	-	+	+	-	-	+	+	-	+	+	+	-	+	-	-	+	+	+	52.2
Mortality	+	-	+	-	-	+	-	-	+	+	-	-	+	-	-	-	-	-	+	+	-	+	-	39.1

Table 2. Antimicrobial susceptibility of *S. maltophilia* isolates.

Antibiotic	Susceptibility	
	n	(%)
Amikacin	10	(43.5)
Gentamicin	8	(34.8)
Tobramycin	9	(39.1)
Ceftazidime	6	(26.1)
Cefepime	5	(21.7)
Ciprofloxacin	11	(47.8)
Piperacillin/tazobactam	11	(47.8)
Ticarcillin/clavulanate	17	(73.9)
Trimethoprim/sulfamethoxazole	23	(100)

subsequently been proved that, as an opportunist pathogen, it causes infections with serious courses, particularly in immunosuppressive and weak patient groups (3,4,8). Clinically significant infection with *S. maltophilia* is uncommon among healthy individuals. The bacterium causes endocarditis, pneumonia, meningitis, spinal-epidural abscesses, conjunctivitis, keratitis, corneal ulcers, mastoiditis, epididymitis, urinary and gastrointestinal infections, and bloodstream infections (8-11). Recent reports have determined an increased risk of contracting the pathogen in patients treated with broad-spectrum antimicrobial agents (3). The fact that all our patients used broad spectrum antimicrobial agents was a risk factor for *S. maltophilia*.

Patients' length of hospitalization is also, as in our study, a risk factor for *S. maltophilia* infection (12,13). Therefore, discharging patients as soon as possible will reduce *S. maltophilia* infections and health care associated infections caused by other agents.

Immunosuppression and malignancy are other well-known risk factors for *S. maltophilia* infection (3,14). In our study, immunosuppression and malignancy were present in most patents with *S. maltophilia* pneumonia. Therefore, patients with immunosuppression and malignancy should be monitored more carefully.

Curing infections stemming from *S. maltophilia* is hard due to the bacterium's higher resistance levels. Trimethoprim-sulfamethoxazole, ticarcillin/ clavulanate, doxycycline, and new quinolones are reported to be the most active agents against *S. maltophilia* (3,15-18).

While the most sensitive antibiotics in *S. maltophilia* isolation were trimethoprim-sulfamethoxazole and ticarcillin/clavulanate, their sensitivity levels were very low compared to those of other antimicrobial agents (3). Because of their high resistance to the antibiotics used against health care associated infections, the infections thriving with this micro-organism have high morbidity and mortality rates. In our study mortality was 39.1%. Similar rates have been determined in other reports of infection with *S. maltophilia* (19,20). The most important reason for such high mortality rates is that the appropriate empiric antibiotics are frequently not administered (21).

Appropriate empiric antibiotics were administered to only 12 patients; on the other hand, the mortality rate in those patients to whom appropriate empiric antibiotics was not administered was high, which proves that suitable empiric therapy is vitally important. In addition, and especially in nosocomial pneumonia cases, not taking sputum or BAL samples from patients or delays in taking such samples inhibits appropriate therapy.

In conclusion, *S. maltophilia*, similar resistant microorganisms, and health care associated infections must be combated before infections emerge; therefore, active infection control programs and rational antibiotics usage policies must be put in place. If infection still occurs despite all these measures and the risk factors for *S. maltophilia* infection (neutropenic, hematologic malignancy, use of broad spectrum antibiotics, immunosuppression, prolonged hospitalization and intravenous catheter use, etc.) still apply, trimethoprim-sulfamethoxazole should be available from among the empiric antibiotics that can be selected.

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