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ORIGINAL ARTICLE

Risk factors associated with *Sphingomonas paucimobilis* infection

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KEYWORDS

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Background: *Sphingomonas paucimobilis* is rarely isolated from clinical specimens and it is associated with a great variety of infections. The aim of this study is to investigate the microbiological and clinical features of *S paucimobilis* infection in southern Taiwan.

Methods: *S paucimobilis* isolates from the microbiology laboratory of Chi-Mei Medical Center and their relevant clinical data from October 2005 to October 2009 were retrospectively reviewed.

Results: A total of 55 patients with documented *S paucimobilis* infections were identified. Among them, 29 (52.7%) have community-acquired infections and 13 of them presented with primary bacteremia (44.8%). Multivariate logistic regression showed that community-acquired infection [adjusted odds ratio 13.473, 95% confidence interval (CI) 1.79–101.41, $p = 0.01$], diabetes mellitus (adjusted odds ratio 7.03, 95% CI 1.16–42.66, $p = 0.03$), and alcoholism (adjusted OR 10.87, 95% CI 1.00–117.69, $p = 0.05$) were significant risk factors for *S paucimobilis* primary bacteremia. Most of those who have health care-associated *S paucimobilis* infections presented with pneumonia (10 of 26, 38.5%) and only 7.7% presented with catheter-related infection. The overall mortality rate was 5.5%.

Conclusion: Community-acquired *S paucimobilis* infections were not uncommon, mainly presenting with primary bacteremia. Multivariate analysis showed that community-acquired infection, diabetes mellitus, and alcoholism were significant risk factors for primary bacteremia. Copyright © 2011, Taiwan Society of Microbiology. Published by Elsevier Taiwan LLC. All rights reserved.

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Introduction

Sphingomonas paucimobilis (formerly known as *Pseudomonas paucimobilis* and CDC group Ilk-1) is a strictly aerobic, nonspore-forming, nonfermentative Gram-negative bacillus. It is characterized by catalase and oxidase activity, yellow pigment production, and slow motility with single polar flagellum.¹ This organism is ubiquitous in the natural environment (especially in water and soil), and it is used for bioremediation of the environment for its ability to decompose aromatic compounds.² It has also been recovered from diverse sources in the hospital environment, including hospital water system, respiratory therapy equipment, and laboratory instruments. Nosocomial outbreaks of *S paucimobilis* have been reported and considered to originate from contaminated hospital environment and equipment.^{3–5}

S paucimobilis is an opportunistic pathogen and identification of the organism from clinical specimen is rare. It has been isolated from blood, sputum, urine, wound, bile, cerebrospinal fluid, vagina, and cervix. A great variety of community-acquired and health care-associated infections have been reported, in which catheter-related infection is the most common form.⁶ Although *S paucimobilis* infection occurred occasionally at our hospital, case mortality had been noted. The aim of this study is to investigate the clinical features, risk factors, and outcomes of patients with *S paucimobilis* infection in a tertiary hospital in southern Taiwan.

Materials and methods

Setting

This study was performed at a 1,200-bed tertiary hospital in southern Taiwan. All of the clinical specimens in this hospital are handled by a central microbiology laboratory.

Patients

Clinical data were collected retrospectively from the medical records of patients with documented *S paucimobilis* infection from October 2005 to October 2009. Relevant data obtained included demographic characteristic, underlying disease, comorbidity, clinical presentation, recent invasive procedure, infection source, laboratory data, bacteriology data, and clinical outcome.

Bacterial identification and antimicrobial susceptibility testing

These organisms were identified from various clinical specimens with the use of Bactec Model 9240 (Becton-Dickinson, Sparks, MD, USA) or the API 20NE system (bio-Mérieux, Marcy L'Etoile, France). Susceptibility testing of these isolates to eight antimicrobial agents was performed with the use of disk diffusion method. These agents included ceftazidime, cefpirome, imipenem-cilastatin, ciprofloxacin, gentamicin, amikacin, piperacillin-tazobactam, and sulfamethoxazole-trimethoprim (SMX-TMP). *Staphylococcus aureus* (American Type Culture Collection)

ATCC 25923, *Escherichia coli* ATCC 25922, and *Pseudomonas aeruginosa* ATCC 27853 were used as control strains in the tests. The breakpoints of susceptibility were according to the recommendation of Clinical and Laboratory Standards Institute.⁷

Definitions

S paucimobilis infection was defined as a patient presented with systemic inflammatory response syndrome and a positive culture for *S paucimobilis*. Primary bacteremia was defined as *S paucimobilis* bacteremia with signs of sepsis but without an identifiable focus of infection. Catheter-related infection was indicated by a positive blood culture without an apparent source of bacteremia except the central venous catheter. Fluid or pus aspirated from deep tissue or abscess (excluding body fluid) was regarded as soft tissue infection. However, a positive culture of a superficial wound swab was considered as colonization, in the absence of systemic inflammatory response syndrome. Positive culture of specimens obtained from head and neck region, including surgical specimen and fine needle aspiration, were regarded as head and neck infection. Pneumonia is diagnosed by clinical symptoms and chest X-ray findings. The sputum culture was defined as colonization if Gram stain yields more than 10 epithelial cells per low-power field or less than 25 polymorphonuclear cell per low-power field.

Health care-associated infection was defined as an infection that developed in a patient at least 48 hours after hospitalization, with the organism being isolated from an obviously infected focus. Antibiotic therapy was defined as inappropriate if an antibiotic agent active against *S paucimobilis* (as determined by *in vitro* susceptibility testing) was not administered during the first 48 hours after the diagnosis of infection.

Statistical analyses

Comparisons between groups were made with χ^2 or Fisher's exact test for categorical variables and Student *t* test for continuous variables. A *p* value <0.05 was considered significant. Comparison between patient with primary bacteremia and nonprimary bacteremia was done to identify risk factors for primary bacteremia. Risk factors with a *p* value less than 0.1 were chosen for multivariate logistic regression, using stepwise forward method. Age, gender, and malignancy (which has been reported as a risk factors for bacteremia)⁸ were also included for multivariate analysis. Analyses were performed using commercial statistical software SPSS version 13.0 (SPSS Inc., Chicago, IL, USA).

Results

Demographic characteristics

A total of 63 isolates of *S paucimobilis* were identified from 61 patients from October 2005 to October 2009 in our hospital. Their medical records were reviewed and six patients were excluded because of colonization only (two wound swabs and four sputum specimens). Only

nonduplicate isolates were included for analysis. Consequently, 55 patients with documented *S paucimobilis* infection were included in this study. The data was summarized in Table 1.

Among these patients, 29 patients (52.7%) have community-acquired *S paucimobilis* infection, whereas the rest has health care-associated infections. Primary bacteremia (27.3%) was the most common type of infection, followed by pneumonia (21.8%) and head and neck infection (21.8%). There were only two cases of catheter-related infections.

Comparisons between community-acquired and health care-associated infections were summarized in Table 1. Significantly, more patients presented with primary bacteremia in community-acquired group (44.8% vs. 7.7%, $p < 0.01$) and with pneumonia in health care-associated group (38.5% vs. 6.9%, $p = 0.01$). The health care-associated group had more patients with underlying chronic heart disease (26.9% vs. 3.4%, $p = 0.02$).

Potential risk factors were compared between patient with primary bacteremia and nonprimary bacteremia (Table 2), a p value of less than 0.05 was used to identify the risk factors. This univariate analysis revealed community-acquired infection ($p < 0.01$), diabetes mellitus ($p = 0.01$), and alcoholism ($p < 0.01$) as risk factors for *S paucimobilis* primary bacteremia (Table 2). In addition,

steroid usage ($p = 0.06$), age, gender, and malignancy were also included for multivariate logistic regression analysis, which showed that community-acquired infection [adjusted odds ratio 13.47, 95% confidence interval (CI) 1.79–101.41, $p = 0.01$], diabetes mellitus (adjusted OR 7.03, 95% CI 1.16–42.66, $p = 0.03$), and alcoholism (adjusted OR 10.87, 95% CI 1.00–117.69, $p = 0.05$) were significant risk factors for primary bacteremia (Table 3).

Antimicrobial susceptibility testing

Susceptibility of *S paucimobilis* varied from 72.7% to 94.5% for all the antimicrobial agents tested (Table 4). Of note, 3 of 55 (5.5%) isolates of *S paucimobilis* were resistant to imipenem-cilastatin. Community-acquired isolates had a significantly lower susceptibility to SMX-TMP than health care-acquired isolates (72.4% vs. 96.2%, $p = 0.03$).

Treatment and outcome

Most patients received inappropriate antibiotics initially (42 of 55, 76.4%) but were switched to appropriate antibiotics after the availability of culture results and susceptibility testing. Cure was achieved in the two cases with catheter infection with appropriate antibiotics, and one required

Table 1 Demographic characteristics and clinical manifestations of 55 patients with *S paucimobilis* infections

Characteristics	All, n (%)	Community-acquired, n (%)	Health care-associated, n (%)	p^a
Patients	55	29	26	
Age (mean \pm SD)	50.0 \pm 25.6	43.9 \pm 22.9	56.8 \pm 27.1	0.06
Gender (male)	34 (61.8)	19 (65.5)	15 (57.7)	0.55
Source of infection				
Primary bacteremia	15 (27.3)	13 (44.8)	2 (7.7)	<0.01
Catheter-related infection	2 (3.6)	0	2 (7.7)	0.21
Pneumonia/empyema	12 (21.8)	2 (6.9)	10 (38.5)	0.01
Urinary tract infection	2 (3.6)	0	2 (7.7)	0.22
Soft tissue infection	10 (18.2)	7 (24.1)	3 (11.5)	0.30
CNS infection	2 (3.6)	1 (3.4)	1 (3.8)	1.00
Head and neck infection	12 (21.8)	6 (20.7)	6 (23.1)	0.83
Underlying diseases				
Diabetes mellitus	13 (23.6)	7 (24.1)	6 (23.1)	0.93
Malignancy	8 (14.5)	5 (17.2)	3 (11.5)	0.71
Chronic heart disease	8 (14.5)	1 (3.4)	7 (26.9)	0.02
Chronic lung disease	5 (9.1)	2 (6.9)	3 (11.5)	0.66
Chronic kidney disease	0	0	0	—
Cirrhosis	3 (5.5)	2 (6.9)	1 (3.8)	1.00
Steroid usage	4 (7.3)	3 (10.3)	1 (3.8)	0.61
Alcoholism	6 (10.9)	5 (17.2)	1 (3.8)	0.20
Treatment				
Inappropriate	42 (76.4)	24 (82.8)	18 (69.2)	0.24
Complications/outcomes				
Septic shock	5 (9.1)	3 (10.3)	2 (7.7)	1.00
Acute respiratory failure	14 (25.5)	4 (13.8)	10 (38.5)	0.06
Acute renal failure	6 (10.9)	1 (3.4)	5 (19.2)	0.09
ICU stay	15 (27.3)	4 (13.8)	11 (42.3)	0.03
Mortality	3 (5.5)	1 (3.4)	2 (7.7)	0.60

^a Comparison between community-acquired infection and health care-associated infection.

CNS = central nervous system; ICU = intensive care unit; SD = standard deviation.

Table 2 Characteristics of patients with primary bacteremia caused by *S paucimobilis*

Characteristics	Primary bacteremia, n (%)	Nonprimary bacteremia, n (%)	p
Patients	15	40	
Age (mean ± SD)	55.2 ± 28.1	48.0 ± 24.6	0.35
Gender (male)	8 (53.3)	26 (65.0)	0.43
Source of patient			
Community acquired	13 (86.7)	16 (40.0)	<0.01
Underlying diseases			
Diabetes mellitus	7 (46.7)	6 (15.0)	0.01
Malignancy	3 (20.0)	5 (12.5)	0.67
Chronic heart disease	3 (20.0)	5 (12.5)	0.67
Chronic lung disease	3 (20.0)	2 (5.0)	0.12
Cirrhosis	2 (13.3)	1 (2.5)	0.18
Steroid usage	3 (20.0)	1 (2.5)	0.06
Alcoholism	5 (33.3)	1 (2.5)	<0.01
Complications and outcomes			
Septic shock	2 (13.3)	3 (7.5)	0.61
Acute respiratory failure	2 (13.3)	12 (30.0)	0.30
Acute renal failure	0	6 (15.0)	0.17
ICU stay	2 (13.3)	13 (32.5)	0.19
Mortality	0	3 (7.5)	0.55

ICU = intensive care unit; SD = standard deviation.

removal of the catheter, whereas the other patient retained his Port-A catheter.

Five (9.1%) of the patients had septic shock, 14 (25.5%) had acute respiratory failure, and 6 (10.9%) had acute renal failure. A larger portion of the patients in health care-associated group required intensive care (42.3% vs. 13.8%, $p = 0.03$). There was no difference in the incidence of complication between the two groups. Despite inappropriate initial antibiotic treatment and development of complication, the overall mortality rate was low (3 of 55, 5.5%). One of them was a 58-year-old man with diabetes, who presented to the emergency department with disturbance of consciousness and subsequent culture of the cerebrospinal fluid yielded *S paucimobilis*. The patient died of septic shock with multiorgan failure (including acute renal failure and disseminated intravascular coagulation) after 10 days. The other two patients were a 22-year-old woman with seizure disorder and a 48-year-old man with intracerebral hemorrhage, and both developed *S paucimobilis* ventilator-associated pneumonia during hospitalization.

Discussion

S paucimobilis was first reported to cause human infection in 1979 and was named *Pseudomonas paucimobilis*. It was renamed *Sphingomonas paucimobilis* in 1990 based on phylogenetic data.¹ It is well known as a waterborne organism and its infections being attributable to contaminated water sources have been reported.^{9–11} *S paucimobilis* can cause a variety of infections in both healthy people and immunocompromised hosts. Clinical syndrome associated with *S paucimobilis* include primary bacteremia, intravascular catheter infections, peritoneal dialysis-associated peritonitis,¹² urinary tract infection, biliary tract infection, cutaneous infection,¹³ ventilator-associated pneumonia,¹⁴ meningitis,¹⁵ myositis,¹⁶ osteomyelitis,¹⁷ septic arthritis,^{18,19} endophthalmitis,^{20,21} cervical adenitis,⁹ bromhidrosis,²² and diarrheal disease.⁶ Most *S paucimobilis* infections reported in the literature were either hospital acquired or related to nosocomial outbreaks.^{3–5,23–26} In our study, 52.7% of our patients have community-acquired infection, which is much higher than

Table 3 Multivariate analysis of risk factors for acquiring primary bacteremia caused by *S paucimobilis*

Risk factors	Multivariate analysis		p
	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI) ^a	
Community-acquired	9.75 (1.93–49.15)	13.47 (1.79–101.41)	0.01
Diabetes mellitus	4.958 (1.31–18.84)	7.03 (1.16–42.66)	0.03
Alcoholism	19.5 (2.04–186.24)	10.87 (1.00–117.69)	0.05

^a Odds ratio adjusted for age, gender, steroid use, and malignancy. CI = confidence interval.

Table 4 Antimicrobial susceptibility of 55 strains of *S paucimobilis*

Antibiotics	All, n (%)	Community-acquired, n (%)	Health care-associated, n (%)	<i>p</i> ^a
Ceftazidime	42 (76.4)	24 (82.8)	18 (69.2)	0.23
Cefpirome	43 (78.2)	25 (86.2)	18 (69.2)	0.19
Piperacillin-tazobactam	40 (72.7)	19 (65.5)	21 (80.7)	0.21
Imipenem-cilastatin	52 (94.5)	28 (96.6)	24 (92.3)	0.60
Ciprofloxacin	41 (74.5)	22 (75.9)	19 (73.1)	0.81
Gentamicin	48 (87.3)	24 (82.8)	24 (92.3)	0.43
Amikacin	50 (90.9)	25 (86.2)	25 (96.2)	0.36
SMX-TMP	46 (83.6)	21 (72.4)	25 (96.2)	0.03

^a Comparison between community-acquired infection and health care-associated infection. Among the 55 strains, 29 strains were isolated from community-acquired infection and the remaining 26 strains were from health care-associated infections. SMX-TMP = sulfamethoxazole-trimethoprim.

those reported previously (9.7%–31.0%).^{6,8} Most of the community-acquired infection presented with primary bacteremia (13 of 29, 44.8%) and mainly occurred in immunocompromised hosts.

According to Cheong et al.,⁶ the most common type of infection was catheter-related infection (34.8%) followed by primary bacteremia (26.1%), continuous ambulatory peritoneal dialysis peritonitis (13.0%), and gastrointestinal infection (8.7%). However, among our patients with health care-associated *S paucimobilis* infection, the most common presentation was pneumonia and most of them were ventilator-associated pneumonia.

S paucimobilis bacteremia had been reported mainly in patients with indwelling devices or in immunocompromised host, especially those with neutropenia^{11,27} and hematopoietic stem cell transplantation.^{26,28,29} A recent study by Lin et al.⁸ focused on *S paucimobilis* bacteremia stated that the most common comorbidities were malignancy (57.1%) and immunosuppressant use (40.5%). However, the most common comorbidities of their own series were malignancy (56.3%) and diabetes mellitus (31.3%). Although there was a higher rate of catheter-related bloodstream infection (33.3%) after cases combining with the literature, the incidence rate of their own series was 18.8% (3 of 16). In contrast, in our study, there were only two cases of catheter-related infection. Most of our patient with bacteremia presented with primary bacteremia and most of them were categorized as community-acquired infections. Multivariate logistic regression showed that community-acquired infection, diabetes mellitus, and alcoholism were risk factors for primary bacteremia of *S paucimobilis* infection. Based on a geographical study of the nationwide distribution of melioidosis in Taiwan, southern Taiwan has the highest rate of positivity of *Burkholderia pseudomallei* in soil samples and the highest prevalence of the disease.³⁰ Our series has a higher percentage of community-acquired *S paucimobilis* infections compared with other studies.^{3,6,8} Whether there is any geographical difference in distribution of this pathogen in the environment (water or soil) required further study.

Most of the strains of *S paucimobilis* in this survey are usually susceptible to aminoglycosides, carbapenems, and SMX-TMP. They are usually resistant to penicillins and first-generation cephalosporins because of the production of chromosomally encoded beta-lactamase production.³¹

However, susceptibility to the third-generation cephalosporins and fluoroquinolones varied. The resistance rates of *S paucimobilis* to various antibiotics in our study are similar to previous study.^{6,8} Only three isolates of *S paucimobilis* were imipenem resistant but remained susceptible to cefpirome, amikacin, and SMX-TMP. A high rate of resistance to SMX-TMP was found in the community strains compared with health care-associated strains (27.4% vs. 3.8%, *p* = 0.03). Whether this is a result of selection pressure from the wide usage of SMX-TMP in treating common community-acquired infections needs more investigations to provide a plausible explanation.

Aminoglycoside plus a third-generation cephalosporin have been recommended as suitable antibiotics for treatment of *S paucimobilis* infections in previous study.³ In our study, carbapenem may be another good treatment choice because of its high susceptibility rate (94.5%) for *S paucimobilis*. Besides, for those who had catheter-related infections (including those with peritoneal dialysis-related peritonitis), catheter removal is suggested if poor clinical response to medical therapy is noted, although good clinical outcome without catheter removal has been reported.⁶

Among our patient, 9.1% (5 of 55) of them developed septic shock during presentation. In contrast, 18.8% (3 of 16) of the patients in the study by Lin et al.⁸ also had septic shock as a result of *S paucimobilis* bacteremia. Despite the probability of development of complications, the overall prognosis of *S paucimobilis* infection is usually favorable. Although more patients with health care-associated infection requiring intensive care in our study, there was no statistical difference about the development of complications between community-acquired and health care-associated *S paucimobilis* infections.

In a study done in Korea, less than half (10 of 23, 43.5%) of the patients received inappropriate initial empirical antibiotic therapy.⁶ All patients survived despite inappropriate initial antimicrobials. Most (76.4%) of our patients received inappropriate antibiotics initially. Although two of the three deceased patients received inappropriate antibiotics initially, the overall outcome for patients with inappropriate antibiotics was favorable with a survival rate of 95.2% (40 of 42). The mortality in our case series was believed to be associated to the underlying diseases of the patients rather than inappropriate therapy. Although fatal cases were noted in our patients, *S paucimobilis* was

considered to have limited virulence,³² probably related to the lack of lipopolysaccharide A in its cell wall.³³ These findings may explain the relatively favorable clinical outcome of the patients with *S paucimobilis* infections.

In conclusion, community-acquired *S paucimobilis* infections are not uncommon, mainly present with primary bacteremia. Univariate and multivariate analysis showed that community-acquired infection, diabetes mellitus, and alcoholism were significant risk factors for primary bacteremia. These findings markedly contrasted with those of previous studies from other countries. The association between much higher probability of community-acquired *S paucimobilis* infection and environmental exposure is worth further study.

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