J Microbiol Immunol Infect 2010;43(1):35–42

Contents lists available at ScienceDirect

Journal of Microbiology, Immunology and Infection

Journal homepage: http://www.e-jmii.com

Original Article

Sphingomonas paucimobilis Bacteremia in Humans: 16 Case Reports and a Literature Review

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BACKGROUND/PURPOSE: *Sphingomonas paucimobilis* is a glucose-nonfermenting Gram-negative bacillus that is widely distributed in both natural environment and hospitals. Various infections in humans have been reported, but most have been limited to sporadic case reports. The aim of this study was to describe the clinical characteristics and manifestations of *S. paucimobilis* bacteremia. We also reviewed the literature on *S. paucimobilis* bacteremia.

METHODS: Cases of *S. paucimobilis* bacteremia were identified retrospectively at a university-affiliated hospital in Taiwan. In addition, relevant case reports were identified through PubMed and reviewed.

RESULTS: From April 2004 to April 2008, 42 cases of *S. paucimobilis* bacteremia were identified in this study. Among them, 16 cases were identified from E-Da hospital, Kaohsiung, Taiwan and 26 cases from the literature review. The median age of patients was 48.5 years and 57.1% were male. The most common comorbidities included malignancy (57.1%), immunosuppressant use (40.5%), and diabetic mellitus (11.9%). Hospital-acquired bacteremia accounted for 69.0% of infections. Primary bacteremia and catheter-related bloodstream infection were found in 35.7% and 33.3% respectively. The most effective antibiotics were fluoroquinolones, carbapenems, and β-lactam/β-lactamase inhibitor combinations. All 42 patients survived the *S. paucimobilis* bacteremic episodes, but three patients experienced septic shock.

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Article History:
Received: Sep 30, 2008
Revised: Jan 21, 2009
Accepted: Feb 17, 2009

CONCLUSION: *S. paucimobilis* can cause infections in healthy as well as immunocompromised individuals. Although it is an organism of low clinical virulence, infection caused by *S. paucimobilis* can lead to septic shock. Further clinical research is required to characterize this infection.

KEYWORDS: antibiotic treatment, bacteremia, septic shock, *Sphingomonas paucimobilis*

Introduction

Sphingomonas paucimobilis, formerly known as *Pseudomonas paucimobilis*, is a yellow-pigmented, glucose-nonfermenting, strictly aerobic, Gram-negative bacillus with a single polar flagellum. It is categorized as CDC group IIk biotype 1,[1] and it was initially reported to be a human pathogen in 1979.[2–4] The natural habitat of this organism has not been fully defined but it is known to be widely distributed in the natural environment, particularly in water and soil, and has also been isolated from hospital settings, including hospital water systems, distilled water, dialysis fluid, nebulizers, and other respiratory therapy equipment.[5–8] *S. paucimobilis* has been associated with a variety of infections in humans, including bacteremia, pneumonia, catheter-related infections, meningitis, peritonitis, osteomyelitis, septic arthritis, postoperative endophthalmitis, lung empyema, splenic abscesses, urinary tract infections, and biliary tract infections.[3,4,9–28]

S. paucimobilis bacteremia occurs infrequently, but it has been encountered with increasing frequency in clinical settings. The only current publications discussing *S. paucimobilis* bacteremia are either isolated case reports or short series reports. In this study, we analyzed the clinical characteristics, manifestations, treatment, and clinical outcome of patients with *S. paucimobilis* bacteremia, identified both from E-Da hospital, Kaohsiung, Taiwan and the literature review. To the best of our knowledge, this is the largest case study of *S. paucimobilis* bacteremia to date.

Methods

Patient identification

This retrospective study was conducted at the E-Da hospital, a 1,000-bed hospital affiliated to I-Shou University in Southern Taiwan, and has been approved by the institutional review board of E-Da hospital (No. EMRP-097-026). From April 2004 to April 2008, the medical records of patients with positive blood cultures for *S. paucimobilis* were reviewed. Only patients with notable infections, such as fever, leukocytosis, or other laboratory findings evidenced by radiographic, surgical, or clinical findings, were included in this study. Demographic and clinical data were collected, including age, gender, underlying diseases, vital signs, indwelling intravenous devices, antimicrobial chemotherapy, and clinical outcomes.

Definition of bacteremia

Hospital-acquired bacteremia was defined by at least one positive blood culture for *S. paucimobilis* taken at least 72 hours after admission in patients without clinical evidence of septicemia on presentation. Community-acquired bacteremia was defined in patients that developed bacteremia within 72 hours of hospitalization. The source of bacteremia was determined on the basis of clinical findings or bacterial culture results. Bacteremic episodes without concurrent infectious foci were considered as primary bacteremia. Types of indwelling intravascular devices included the central venous pressure catheter, Hemo-Cath, Port-A-Cath, Hickman catheter, Dacron graft, Groshong catheter, and arterial line. Catheter-related bacteremia was diagnosed according to the standard definitions of catheter-related infections: (1) isolation of the same microorganism from blood and exudates from the catheter exit site or specimens from the catheter lumen in the presence of signs of inflammation; and (2) isolation of the same microorganism from blood and the catheter tip on removal of the catheter.[29] Shock was defined as systolic blood pressure <90 mmHg or requiring inotropic agents to maintain blood pressure. Immunosuppressant use was defined as the utilization of cytotoxic agents for cancer, before bone marrow transplantation, or the use of corticosteroids (>30 mg prednisolone daily or 1 week). We defined antibiotic therapy as inappropriate if an antibiotic agent active against *S. paucimobilis* (as determined by *in vitro* susceptibility testing) at the usual recommended dosage was

not administered during the 48 hours after diagnosis of infection.

Microbiology on blood culture samples

Blood culture samples were processed by the BACTEC 9240 system (Becton Dickinson, Sparks, MD, USA). All positive cultures were Gram-stained and subcultured on blood agar and eosin-methylene blue agar plates for further identification. Identification of *S. paucimobilis* was performed on the ID 32 GN (bioMérieux, Marcy L'etoile, France) or Phoenix-100 ID/AST (Becton Dickinson) automated system. All *S. paucimobilis* isolates were tested for antibiotic susceptibility by the standard disk diffusion method. Because there are no standards for the susceptibility test for *S. paucimobilis*, the zone diameter interpretive standards were applied as described for the glucose-nonfermenting bacilli *Acinetobacter* spp. according to the criteria of Clinical and Laboratory Standards Institute (formerly the National Committee for Clinical Laboratory Standards).[30]

Review of the literature

A literature search was initiated through PubMed (National Library of Medicine, Bethesda, MD, USA; database from January 1966 through April 2008) using the following key words: *Sphingomonas paucimobilis* or *Pseudomonas paucimobilis*. Only bacteremic patients were enrolled in our study. The demographic data, clinical characteristics, manifestations, treatments, and clinical outcomes were collected for further analysis.

Results

A total of 16 patients who had positive blood cultures for *S. paucimobilis* were identified from our hospital during the study period. The median age of the patients was 54.0 years (range, 5 month–87 years; Table 1). In the literature search, 26 patients with *S. paucimobilis* bacteremia were identified. The median age of patients was 45.5 years (range, 10 days–82 years; Table 2).[3,4,9–21] Two cases were reported before 1980, two from 1981 to 1990,

Table 1. Clinical characteristics and manifestations of 16 survived patients with *Sphingomonas paucimobilis* bacteremia

Case	Age	Sex	Infectious foci	Underlying conditions	Acquired source	Intravascular devices	Antibiotics
1	45 yr	M	SSTI	Oral cancer	Community	–	Cefazolin, gentamicin
2	77 yr	M	SSTI	HCC, LC	Community	–	Amoxicillin/clavulanate
3	70 yr	F	BTI	Klatskin tumor, DM	Hospital	–	Piperacillin, gentamicin
4[a]	77 yr	M	Primary	DM, LC, ESRD, HCC	Hospital	Hemo-Cath	Ceftazidime
5	52 yr	F	CR-BSI	Colon cancer	Hospital	Port-A-Cath	Cefoxitin
6	18 yr	F	UTI	ESRD, schizophrenia	Hospital	Hemo-Cath	Cefazolin
7	62 yr	F	Primary	Ureteral stone	Community	–	Cefuroxime
8	87 yr	F	Primary	Radial fracture, DM	Hospital	–	Cefuroxime, gentamicin
9	5 yr	M	Pneumonia	–	Community	–	Ampicillin/sulbactam
10	56 yr	F	CR-BSI	Colon cancer, COPD, chronic steroid use	Hospital	Port-A-Cath	Cefotaxime, gentamicin
11	60 yr	F	Primary	DM, chronic steroid use	Hospital	–	Ceftazidime
12	76 yr	F	Pneumonia	Chronic steroid use	Hospital	–	Ceftazidime
13	48 yr	M	SSTI	Hypopharyngeal cancer	Hospital	–	Piperacillin, amikacin
14	49 yr	M	CR-BSI	Oral cancer, HCC, LC, DM	Hospital	Port-A-Cath	Cefazolin, gentamicin
15	5 mo	M	UTI	–	Community	–	Ampicillin, gentamicin
16	43 yr	M	Primary	Esophageal cancer, alcoholism	Community	Port-A-Cath	Cefazolin, gentamicin

[a]Patient presented with septic shock. SSTI = skin and soft tissue infection; HCC = hepatocellular carcinoma; LC = liver cirrhosis; BTI = biliary tract infection; DM = diabetes mellitus; ESRD = end-stage renal disease; CR-BSI = catheter-related bloodstream infection; UTI = urinary tract infection; COPD = chronic obstructive pulmonary disease.

Table 2. Clinical characteristics and manifestations of 26 survived patients with *Sphingomonas paucimobilis* bacteremia from the literature review

Case	Age	Sex	Infectious foci	Underlying conditions	Acquired source	Intravascular devices	Antibiotics	Ref.
1	39 yr	M	Meningitis	Epilepsy	Community	–	INH, RIF, SM	3
2	79 yr	M	Pneumonia	Pulmonary embolization, Af	Hospital	–	Ampicillin	4
3	61 yr	M	SSTI	Aorto-bifemoral bypass, alcoholism, narcotic abuse	Hospital	Dacron graft	Cephalothin, erythromycin, tobramycin	9
4	72 yr	F	Pneumonia	COPD, steroid use	Community	–	Cefotaxime, amikacin	10
5	82 yr	M	Primary	ESRD	Community	–	Vancomycin, amikacin	11
6	47 yr	M	Primary	LC, alcoholism	Community	–	Cefotaxime, tobramycin	12
7	6 yr	M	Primary	None	Community	–	Cefotaxime, gentamicin	12
8	30 yr	F	Primary	AIDS	Community	Groshong catheter	Ceftazidime, amikacin	13
9	67 yr	M	Primary	Bladder carcinoma	Community	Groshong catheter	Ceftazidime, TMP/SMZ	13
10[c]	64 yr	F	Primary	Alcoholism, burn	Hospital	Intravascular catheter[d]	Ceftazidime, ceftizoxime	14
11	51 yr	M	CR-BSI	Multiple myeloma, PBSCT	Hospital	Hickman catheter	Imipenem, amoxicillin/ clavulanate	15
12	21 yr	M	CR-BSI	NHL, PBSCT	Hospital	Hickman catheter	Imipenem, amikacin, ceftazidime, ciprofloxacin	15
13	44 yr	F	CR-BSI	Perforated appendicitis	Hospital	CVC	Ampicillin, gentamicin, ciprofloxacin	16
14	–[a]	F	–[b]	Breast cancer, PBSCT	Hospital	Intravascular catheter[d]	Fluoroquinolone	17
15	–[a]	F	–[b]	Breast cancer, PBSCT	Hospital	Intravascular catheter[d]	Fluoroquinolone	17
16	–[a]	M	–[b]	Multiple myeloma, PBSCT	Hospital	Intravascular catheter[d]	Fluoroquinolone	17
17	–[a]	M	–[b]	Lymphoma, PBSCT	Hospital	Intravascular catheter[d]	Fluoroquinolone	17
18	48 yr	M	BTI	Cholangiocarcinoma	Hospital	None	N/A	18
19	10 d	M	CR-BSI	Prematurity, respiratory distress	Hospital	Arterial-line	N/A	18
20	78 yr	F	CR-BSI	Ovarian cancer, C/T	Hospital	Port-A-Cath	N/A	18
21	57 yr	F	CR-BSI	ALL, C/T	Hospital	Chemo-Cath	Piperacillin, ceftazidime, netilmicin	19
22[c]	14 yr	M	CR-BSI	AML, BMT	Hospital	CVC	Piperacillin-tazobactam, meropenem, gentamicin	20
23	11 yr	M	Primary	NHL, C/T	Hospital	Hickman catheter	Imipenem	21
24	3 yr	M	Primary	AML, BMT	Hospital	Hickman catheter	Imipenem	21
25	6 yr	F	Primary	Lymphoma, C/T	Hospital	Hickman catheter	Imipenem	21
26	5 yr	F	Primary	Neuroblastoma, C/T	Hospital	Hickman catheter	Imipenem	21

[a]Ages ranged from 22 to 51 years; [b]definite catheter-related infections in two cases, and possible catheter-related infections in two cases; [c]patient survived but with septic shock; [d]unknown type of intravascular catheters. INH=isoniazid; RIF=rifampin; SM=streptomycin; SSTI=skin and soft tissue infection; Af=atrial fibrillation; COPD=chronic obstructive pulmonary disease; ESRD=end-stage renal disease; LC=liver cirrhosis; AIDS=acquired immunodeficiency disease; TMP/SMZ=trimethoprim/sulfamethoxazole; CR-BSI=catheter-related bloodstream infection; PBSCT=peripheral blood stem cell transplantation; NHL=non-Hodgkin's lymphoma; CVC=central venous catheter; BTI=biliary tract infection; N/A=not available; C/T=chemotherapy; ALL=acute lymphocytic leukemia; AML=acute myelocytic anemia; BMT=bone marrow transplantation.

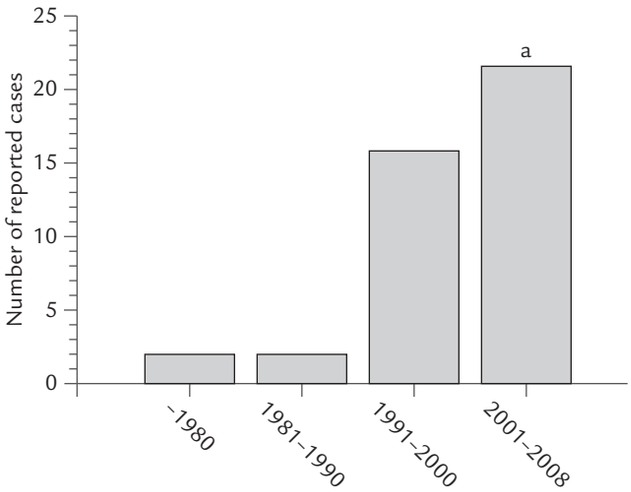

Figure. Number of reported cases of *S. paucimobilis* bacteremia. [a]Include the 16 patients in the present study.

16 from 1991 to 2000, and six were reported after 2001 (Figure).

Combining cases from our patients with those from the literature, we found a total of 42 patients with positive blood cultures for *S. paucimobilis*. The median age was 48.5 years (range, 10 days–87 years) and 57.1% were male (Table 3). Hospital-acquired bacteremia was identified in 69.0% of these patients (62.5% in our hospital and 73.1% in the literature). Of the 42 patients, 25 (59.5%) had indwelling intravenous devices. The most common comorbidities of these patients were malignancy (57.1%), followed by immunosuppressant use (40.5%). Other comorbidities included diabetes mellitus (11.9%), alcoholism (9.5%), liver cirrhosis (9.5%), end-stage renal disease (7.1%), chronic obstructive pulmonary disease (4.8%), burn injury (2.4%), and acquired immunodeficiency syndrome (2.4%). Primary *S. paucimobilis* bacteremia was found in 35.7% of patients. Catheter-related bloodstream infection was identified in 33.3% of patients, skin and soft tissue infection in 9.5%, pneumonia in 9.5%, urinary tract infection in 4.8%, biliary tract infection in 4.8%, and meningitis in 2.4%.

The antimicrobial susceptibility of blood isolates of *S. paucimobilis* from our hospital is summarized in Table 4. The most active antimicrobial agents were levofloxacin (92.9%, 13/14) ciprofloxacin (81.3%, 13/16), ampicillin/sulbactam (81.3%, 13/16), piperacillin/tazobactam (81.3%, 13/16), and imipenem (81.3%, 13/16). Aminoglycosides (gentamicin, amikacin) were also effective against *S. paucimobilis* (75.0%, 12/16). Patients with *S. paucimobilis* bacteremia received diverse antibiotic treatments. Most patients in our hospital received first-, second-, or third-generation cephalosporins, amoxicillin/ampicillin with clavulanate/sulbactam, or piperacillin, combined with or without aminoglycosides. In addition, treatment with fluoroquinolones or carbapenems was also reported in the literature. Of the 16 patients in our hospital, six (37.5%) received inappropriate initial empirical antibiotic therapy. The majority of patients, including those receiving inappropriate initial empirical antibiotic treatment at our hospital and patients from the literature, recovered from *S. paucimobilis* bacteremia. However, three patients (7.4%) suffered septic shock, including one patient from our hospital and two patients from the literature.

Discussion

S. paucimobilis was initially implicated as the causative pathogen in an infectious leg ulcer,[2] but until recently was rarely encountered in clinical settings. However, sporadic case reports indicate that the incidence of infection has been increasing in recent years, and our hospital has identified 16 cases of *S. paucimobilis* bacteremia in the past 4 years. This suggests that *S. paucimobilis* may be an emerging infectious pathogen worthy of further attention.

S. paucimobilis has been isolated from both natural and hospital environments.[5–8] This ubiquitous distribution implicates *S. paucimobilis* in both hospital- and community-based infections. Hospital-acquired infections accounted for 69.0% of patients with *S. paucimobilis* bacteremia in our survey. Most of these patients acquired the infection in the hospital setting secondary to the presence of indwelling intravascular devices. The nosocomial infections are similar to those caused by non-enteric Gram-negative bacilli from hospital water distribution systems which may result in severe infections in patients with underlying debilitating conditions or with indwelling devices.[31] Recurrent and cluster infections have also been reported.[19,21] In our study, we did not type these strains so cannot be sure whether our patients represent an outbreak of a single clone. However, these hospital-acquired bacteremias occurred in different wards and at different times and we therefore propose that these infections are not part of a single outbreak.

Table 3. Demographic characteristics and clinical features among patients with *Sphingomonas paucimobilis* bacteremia[a]

Characteristics	Present study (*n*=16)	Literature (*n*=26)	Total (*n*=42)
Age	54.0 yr (5 mo–87 yr)	45.5 yr (10 d–82 yr)[b]	48.5 yr (10 d–87 yr)[c]
Sex			
male	8 (50.0)	16 (61.5)	24 (57.1)
female	8 (50.0)	10 (39.5)	18 (42.9)
Acquired source			
Hospital	10 (62.5)	19 (73.1)	29 (69.0)
Intravascular devices	6 (37.5)	19 (73.1)	25 (59.5)
Underlying conditions			
Malignancy	9 (56.3)	15 (57.7)	24 (57.1)
Solid	9 (56.3)	6 (23.1)	15 (35.7)
Hematologic	0 (0)	9 (34.6)	9 (21.4)
DM	5 (31.3)	0 (0)	5 (11.9)
ESRD	2 (12.5)	1 (3.8)	3 (7.1)
COPD	1 (6.3)	1 (3.8)	2 (4.8)
Alcoholism	1 (6.3)	3 (11.5)	4 (9.5)
Liver cirrhosis	3 (18.8)	1 (3.8)	4 (9.5)
AIDS	0 (0)	1 (3.8)	1 (2.4)
Burn injury	0 (0)	1 (3.8)	1 (2.4)
Immunosuppressant use	3 (18.8)	14 (53.8)	17 (40.5)
Chronic use of steroid	3 (18.8)	1 (3.8)	4 (9.5)
BMT[d]	0 (0)	8 (30.8)	8 (19.0)
Chemotherapy	0 (0)	5 (19.2)	5 (11.9)
Infectious foci			
CR-BSI	3 (18.8)	11 (42.3)	14 (33.3)
SSTI	3 (18.8)	1 (3.8)	4 (9.5)
BTI	1 (6.3)	1 (3.8)	2 (4.8)
UTI	2 (12.5)	0 (0)	2 (4.8)
Pneumonia	2 (12.5)	2 (7.7)	4 (9.5)
Meningitis	0 (0)	1 (3.8)	1 (2.4)
Primary	5 (31.3)	10 (38.5)	15 (35.7)

[a]Data presented as median (range) or *n* (%); [b]data from 22 patients; [c]data from 38 patients; [d]including two patients with bone marrow transplantation and six patients with peripheral blood stem cell transplantation. DM=diabetes mellitus; ESRD=end-stage renal disease; COPD=chronic obstructive pulmonary disease; AIDS=acquired immunodeficiency syndrome; BMT=bone marrow transplantation; CR-BSI=catheter-related bloodstream infection; SSTI=skin and soft tissue infection; BTI=biliary tract infection; UTI=urinary tract infection.

Bacteremia caused by Gram-negative bacteria frequently results in significant morbidity and mortality rates, especially in patients with nosocomial infections. However, *S. paucimobilis* strains have not been strongly associated with high morbidity or mortality. This survey revealed no deaths due to *S. paucimobilis* bacteremia, but three patients went into septic shock as a result of *S. paucimobilis* bacteremia. Several factors might contribute to the virulence of *S. paucimobilis* in human infections. This organism was found to have a significantly different enzyme profile from that of other bacteria, which may contribute to its pathogenesis.[32] Additionally, the presence of atypical lipopolysaccharide constituents of the outer cellular membrane of *S. paucimobilis* that may correspond to the lipid A present in other Gram-negative bacteria, with the accompanying deficiency in endotoxin activity, has been proposed to explain the low virulence of *S. paucimobilis*.[33] Although *S. paucimobilis* may be considered

Table 4. Antimicrobial susceptibility of blood isolates of *Sphingomonas paucimobilis*[a]

Antimicrobial agent	No. of patients
Ampicillin/sulbactam	13/16 (81.3)
Ceftazidime	11/16 (68.8)
Piperacillin	8/16 (50.0)
Piperacillin/tazobactam	13/16 (81.3)
Gentamicin	12/16 (75.0)
Amikacin	12/16 (75.0)
Ciprofloxacin	13/16 (81.3)
Levofloxacin	13/14 (92.9)
Cefepime	11/16 (68.8)
Imipenem	13/16 (81.3)

[a]Data presented as number of susceptible patients/total patients in present study (%).

to have low virulence, it can still cause life-threatening septic shock, especially in immunocompromised hosts.

No standard method currently exists to determine the antibiotic susceptibility of *S. paucimobilis* and these data are therefore variable in the literature. Peel et al stated that the isolate of *S. paucimobilis* from a leg ulcer was susceptible to tetracycline, kanamycin, gentamicin, sulfamethoxazole, chloramphenicol, carbenicillin, and tobramycin, but resistant to ampicillin, cephalothin, streptomycin, and colistin, as determined by a disk diffusion method.[2] Slotnick et al used disk agar-diffusion testing and revealed that their isolates were sensitive to ampicillin, carbenicillin, chloramphenicol, gentamicin, tobramycin, kanamycin, tetracycline, and cotrimoxazole, and resistant to cephalothin, polymyxin, and nalidixic acid.[4] Smalley et al determined antimicrobial susceptibility by a microbroth dilution method[34] and they reported that all of the isolated *S. paucimobilis* strains produced β-lactamase and were therefore resistant to the majority of cephalosporins and penicillins. Reina et al evaluated the minimal inhibitory concentration of four isolates and observed that all were susceptible to ciprofloxacin and norfloxacin, and they concluded that aminoglycosides and fluoroquinolones should be the clinical antibiotics of choice for *S. paucimobilis* infection in humans.[12] Recently, Kilic et al determined the susceptibility of *S. paucimobilis* to eight antimicrobial agents by E-test (AB BIODISK, Solna, Sweden) and found that all isolates were susceptible to trimethoprim-sulfamethoxazole, imipenem, meropenem, amikacin, cefotaxime, and piperacillin-tazobactam, but 33.3% (2/6 isolates) were resistant to ciprofloxacin and gentamicin.[21] The most effective antimicrobial agents for *S. paucimobilis* isolates *in vitro* in our patients were fluoroquinolones, β-lactam/β-lactamase inhibitor combinations, carbapenems, and aminoglycosides. Most of our patients received first- second-,or third generation cephalosporins or amoxicillin/ampicillin (with or without clavulanate/sulbactam), either combined with aminoglycosides or not, and they all survived *S. paucimobilis* infection, even after receiving inappropriate initial empirical antibiotics. The favorable outcome in our study may support the conclusion that *S. paucimobilis* has low virulence.

There are several limitations in our study. First of all, this is a retrospective study. The treatments administered depended on the physicians' choice. Although all patients survived, it is difficult to compare the effect of different antibiotic treatments. Moreover, since there are no interpretative standards for *S. paucimobilis*, a disk diffusion assay may not be reliable in determining susceptibility and as a treatment guide.

In conclusion, *S. paucimobilis* can cause a variety of infections in healthy as well as immunocompromised individuals. The prevalence of *S. paucimobilis* infection in humans seems to have increased in recent times. This organism is commonly associated with nosocomial infection, especially in patients with indwelling intravascular devices. Although *S. paucimobilis* is an organism of low clinical virulence, infection caused by this pathogen can lead to septic shock, particularly in immunocompromised patients. Therefore, its importance cannot be neglected. Further clinical research is required to characterize this increasingly frequent infection.

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