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Article

Clinical and Microbiological Characteristics of Bacteremia Caused by *Acinetobacter lwoffii*

S.C. Ku, P.R. Hsueh, P.C. Yang, K.T. Luh

Abstract A retrospective study was conducted to analyze the clinical features and pathogenic roles of bacteremia caused by *Acinetobacter lwoffii* during a 4-year period. *Acinetobacter lwoffii* (formerly *Acinetobacter calcoaceticus* var. *lwoffii*) is recognized as normal flora of the skin, oropharynx and perineum of healthy individuals. There are few reports of *Acinetobacter lwoffii* bacteremia associated with indwelling catheters in humans, particularly in immunocompromised hosts. The records of 18 patients with *Acinetobacter lwoffii* bacteremia whose underlying conditions included cancer (11 patients), systemic lupus erythematosus ($n=1$), chronic obstructive pulmonary disease ($n=2$) and other diseases ($n=4$), all but one of whom had indwelling catheters during the bacteremic episode, were examined. The clinical syndromes were classified as probable catheter-related bacteremia ($n=14$), definite catheter-related bacteremia ($n=2$), primary bacteremia ($n=1$) or biliary tract infection ($n=1$). The infections improved after removal of the catheter and/or appropriate antimicrobial therapy. One death was attributable to the bacteremic event. The results of this study show that indwelling catheter-related *Acinetobacter lwoffii* bacteremia in immunocompromised hosts appears to be associated with a low risk of mortality.

Introduction

The recent taxonomy of the genus *Acinetobacter* was proposed by Bouvet and Grimont [1] in 1986 and expanded later [2] to include the seven named genomospecies (*Acinetobacter calcoaceticus*, *Acinetobacter baumannii*, *Acinetobacter haemolyticus*, *Acinetobacter junii*, *Acinetobacter johnsonii*, *Acinetobacter lwoffii* and *Acinetobacter radioresistens*) and nine unnamed genomospecies. *Acinetobacter lwoffii* (formerly known as *Mima polymorpha*, or *Acinetobacter calcoaceticus* var. *lwoffii*) is a nonfermentative aerobic gram-negative bacillus that is ubiquitous in nature and is considered to be normal flora that inhabits the oropharynx, human skin and the perineum and has tropism for urinary tract mucosa [1–3]. It has been suggested that foreign bodies, such as indwelling catheters, play a vital role in the pathogenesis of *Acinetobacter lwoffii* bacteremia [4]. Infections caused by *Acinetobacter lwoffii* in previously reported cases have mostly comprised catheter-related bloodstream infections [5]. There are only few case reports of *Acinetobacter lwoffii* bacteremia in immunocompromised patients [6–8].

In this study, we examined 18 cases of *Acinetobacter lwoffii* bacteremia, the majority of which involved immunocompromised patients who were treated at a tertiary medical center from January 1993 through December 1996. The clinical features and outcomes were reviewed, and the in vitro susceptibility patterns of the isolates to antimicrobial agents were analyzed.

S.C. Ku, P.C. Yang
Department of Internal Medicine, National Taiwan University College of Medicine, National Taiwan University Hospital, 7 Chung-Shan South Road, Taipei, Taiwan

P.R. Hsueh, K.T. Luh (✉)
Department of Laboratory Medicine, National Taiwan University College of Medicine, National Taiwan University Hospital, 7 Chung-Shan South Road, Taipei, Taiwan
e-mail: luhkt@ha.mc.ntu.edu.tw

Patients and Methods

Clinical Features. Reports from January 1993 through December 1996 of blood cultures positive for *Acinetobacter lwoffii* were

reviewed from the Microbiology Laboratory at National Taiwan University Hospital, a 2000-bed teaching hospital serving as a tertiary referral center in northern Taiwan. Medical charts of the patients with blood cultures positive for this organism were analyzed retrospectively using a standardized data-extraction form. The information obtained consisted of demographic data, underlying conditions, indications for hospitalization, the host's immune status, the number of days from hospital admission to the development of bacteremia, types of indwelling catheters, interventions used to treat the bacteremia, such as antibiotic treatment and/or removal of the catheter, duration of fever, clinical syndromes and disease outcome.

Definitions. Clinical syndromes were defined based on the description of Raad and Bodey [4], with modification as definite, possible catheter-related and primary bacteremia. Definite catheter-related bacteremia was defined as a primary bloodstream infection in which there was clinical or acceptable microbiologic evidence implicating the catheter as the source of the infection. The clinical evidence consisted of either an exit-site infection due to the same organism as that isolated from the bloodstream or the resolution of clinical sepsis refractory to antibiotics after the removal of catheters. Acceptable microbiological evidence included isolation of the same organism from the catheter and the bloodstream. Cultures of the catheters were performed by semiquantitative methods as described by Maki et al. [9]. Probable catheter-related bacteremia was defined as the isolation of *Acinetobacter lwoffii* from cultures of at least one blood sample from a patient with clinical manifestations of systemic inflammatory response syndrome [10] and no apparent source of the infection except the catheter. Primary bacteremia was defined as isolation of the organism from the bloodstream without clinical evidence of a portal of entry. Biliary tract infection was defined as clinical signs indicating obstructive jaundice and isolation of the same organism from bile and the bloodstream.

Immunocompromised hosts were defined as patients undergoing corticosteroid therapy and those with associated underlying malignancies, autoimmune diseases and hematologic diseases that impaired immune function. Development of bacteremia after at least 72 h of hospitalization was regarded as a hospital-acquired infection, whereas development of bacteremia earlier than 72 h after admission was regarded as community-acquired. The catheter types were as follows: (i) peripheral intravascular catheter (PIVC); (ii) central intravascular catheter (CIVC), including the Port-A-Cath (Smiths Industries Medical Systems Deltec, USA) and Hickman catheters (Strato Medical/Infusaid, USA) as subgroups of permanent central intravascular catheters; and (iii) percutaneous transhepatic cholangic drainage catheter (PTCDC). Antibiotic therapy was considered appropriate if at least one of the drugs chosen proved to be active against the isolate on the basis of in vitro susceptibility testing results achieved using the standard disk diffusion method.

Bacterial Isolates. Blood specimens of the patients were processed with the Bactec 860 nonradiometric blood culture system (Becton Dickinson, USA). Twenty-six bacterial isolates from the 18 patients were identified by conventional methods [11] and further identified as *Acinetobacter* species by the API 20 NE system (bioMérieux, France) and the Vitek GNI system (bioMérieux Vitek, USA). *Acinetobacter lwoffii* was further differentiated from *Acinetobacter johnsonii* and *Acinetobacter junii* according to the simplified identification scheme of Bouvet and Grimont [12] on the basis of the following: lack of hemolysis on sheep blood agar, negative citrate, lack of growth on L-arginine enriched medium, growth at 37 °C, lack of growth at 41 °C and lack of growth at 44 °C.

Antimicrobial Susceptibility Testing. Susceptibilities of the 26 blood isolates recovered from the 18 patients to 16 antimicrobial agents were determined by the disk diffusion method in accordance with the guidelines of the National Committee for Clinical Laboratory Standards [13].

Results

Clinical Characteristics of Patients. The clinical characteristics of the 18 patients with clinically significant *Acinetobacter lwoffii* bacteremia are summarized in Table 1. Thirteen patients were immunocompromised by their underlying disease (10 with malignancies, 1 with systemic lupus erythematosus, 1 with chronic obstructive pulmonary disease on long-term steroid therapy and 1 with severe aplastic anemia), while the remaining five patients had chronic obstructive pulmonary disease ($n=1$), coronary artery disease associated with decompensated left ventricular function ($n=2$), hemophilia A ($n=1$) and homocystinuria ($n=1$). The period of having the indwelling catheter before the onset of bacteremia ranged from 4 days to 5 months, with PIVCs tending to have been in place for a shorter duration (4 days–$<$2 weeks). Thirteen patients had hospital-acquired bacteremia, including all the patients with PIVCs (patients 2, 11 and 16), and of the five patients who had community-acquired bacteremia (patients 1, 3, 5, 6 and 17), three had permanent CIVCs, one had a PTCDC and one had no indwelling catheter.

Before *Acinetobacter lwoffii* was isolated, eight patients were treated with different combinations of two or more antibiotics that were later shown to be inactive in vitro against the isolates. All except two (patients 10 and 14) of the eight patients survived after removal of the catheter and/or treatment with appropriate antibiotics following the report of positive blood culture. Patient 10 experienced a rapid deterioration of clinical condition and died within 1 day of the bacteremic episode. Patient 14, who had chronic obstructive pulmonary disease with respiratory failure and hypoxic encephalopathy, recovered without appropriate antibiotic treatment or catheter removal. Among the remaining ten patients who were initially treated with appropriate antibiotics, six were kept on antibiotics alone without catheter removal, all of whom recovered after the infectious process. The other four patients who received appropriate antibiotics and had their catheters removed recovered uneventfully. The time until defervescence in patient 12 was 11 days, which was the longest time in the group of patients treated with antibiotics alone. In the group of patients treated with antibiotics and catheter removal, the longest time until defervescence was 13.5 days, experienced by patient 17, in whom removal of the central intravascular catheter was delayed.

Bacterial Isolates. A total of 26 *Acinetobacter lwoffii* isolates were recovered from blood specimens of 18 patients. Five patients (patients 2, 6, 11, 12 and 17) had

Table 1 Demographic, clinical and microbiological features of 18 cases of clinically significant *Acinetobacter lwoffii* bacteremia

Patient no./age (yrs)/sex	Underlying disease	Type of catheter	No. of positive/ total blood cultures	Coisolates (blood/ catheter tip cultures)	Antibiotic treatment after culture result	Removal of the device	Time until deferves-cence	Diagnosis	Out-come
1/62/M	COPD	none	1/2	none/none	ampicillin/ sulbactam	no	16 h	primary bacteremia	S
2/3/M	retinoblastoma, s/p C/T	peripheral	2/3	NFGNB/none	piperacillin, amikacin	yes	12 h	PCRB	S
3/50/F	breast cancer, s/p MRM, C/T	Hickman	1/3	none/none	piperacillin	yes	12 h	DCRB	S
4/52/M	CAD, s/p CABG	central	1/2	none/NFGNB, CNS	amoxicillin/ clavulanate	yes	8 h	PCRB	S
5/36/F	cervical cancer, s/p C/T	Port-A-Cath	1/2	none/none	ceftriaxone, netromycin	no	24 h	PCRB	S
6/50/M	HCC, s/p PTCD	PTCDC	1/2	none/none	cefoperazone, netromycin	yes	undefined[a]	DCRB	S
7/45/F	SLE, CHF, old CVA	central	1/2	none/none	ceftazidime, vancomycin, metronidazole	yes	24 h	PCRB	S
8/87/M	advanced gastric cancer	central	1/2	none/NFGNB	ampicillin/ sulbactam	yes	undefined[a]	PCRB	S
9/60/M	HCC, s/p surgery	central	1/2	none/MSSA	imipenem, fluconazole	yes	24 h	PCRB	R
10/81/M	CAD, old MI, CHF	Swan-Ganz IABP	1/2	none/none	amoxicillin, aztreonam	no	NA[b]	PCRB	D
11/31/M	hemophilia A, hepatitis C	peripheral	3/4	none/none	ampicillin/ sulbactam, ceftazidime	yes	24 h	PCRB	S
12/29/F	acute leukemia, s/p C/T	Port-A-Cath	8/8	none/none	imipenem	no	11 days	PCRB	S
13/36/F	advanced gastric cancer	Port-A-Cath	2/2	none/none	piperacillin, gentamicin	no	4.5 days	PCRB	R
14/82/M	COPD, DM	central	1/2	none/none	ampicillin, netromycin	no	2 days	PCRB	R
15/43/F	breast cancer, s/p C/T	Port-A-Cath	2/2	none/none	ciprofloxacin, tobramycin	no	2.5 days	PCRB	R
16/3/M	homocystinuria	peripheral	1/2	none/none	ceftazidme	yes	2.5 days	PCRB	S
17/6/M	severe aplastic anemia	Hickman	3/3	corynebac-terium/none	amoxicillin/ clavulanate	yes	13.5 days	DCRB	S
18/27/F	acute leukemia, s/p C/T	Port-A-Cath	1/2	none/none	ampicillin/ sulbactam, tobramycin	no	24 h	PCRB	S

[a] Due to discharge during the period of bacteremia and later visits at outpatient clinics

[b] Patient died during the bacteremic episode

COPD, chronic obstructive pulmonary disease; s/p, status post; C/T, chemotherapy; MRM, modified radical mastectomy; CAD, coronary artery disease; CABG, coronary artery bypass graft; HCC, hepatocellular carcinoma; PTCD, percutaneous transhepatic cholangic drainage; SLE, systemic lupus erythematosus; CHF, congestive heart failure; CVA, cerebrovascular accident; MI, myocardial infarction; DM, diabetes mellitus; PTCDC, percutaneous transhepatic cholangic drainage catheter; IABP, intra-aortic balloon pump; NFGNB, nonfermentous gram-negative bacilli; CNS, coagulase-negative staphylococci; MSSA, methicillin-sensitive *Staphylococcus aureus*; PCRB, probable catheter-related bacteremia; DCRB, definite catheter-related bacteremia, NA, not applicable; D, died due to underlying diseases; S, survived and discharged after bacteremic episode; R, recovered from bacteremic episode but died later due to other events

polymicrobial infections. Gram-negative short and long coccobacilli were observed microscopically. These isolates of *Acinetobacter lwoffii* were strictly aerobic and grew well on all common media at 35 °C.

Antimicrobial Susceptibility. The results of in vitro susceptibility testing of the 26 blood isolates by the disk diffusion method are shown in Table 2. All isolates were susceptible to quinolones (ciprofloxacin and ofloxacin). More than 90% of the isolates were susceptible to aminoglycosides, minocycline, amoxicillin/clavulanic acid and imipenem. Susceptibility of these isolates to cephalosporins and aztreonam was low.

Discussion

There has been an increasing incidence of opportunistic nosocomial infection with *Acinetobacter* species in recent decades. Although the clinical course and outcome of *Acinetobacter baumannii* infection are well known [14–18], there have been few reports of *Acineto-*

Table 2 Antimicrobial susceptibility of 26 blood isolates of *Acinetobacter lwoffii*

Antimicrobial agent	No. (%) of susceptible isolates/ no. of isolates tested	
Minocycline	26/26	(100)
Ampicillin	1/14	(7)
Amoxicillin/clavulanate	13/14	(93)
Piperacillin	17/23	(74)
Ticarcillin/clavulanate	15/26	(58)
Imipenem	24/25	(96)
Aztreonam	8/26	(31)
Cefmetazole	0/13	(0)
Ceftazidime	15/26	(58)
Cefoperazone	6/26	(23)
Ceftriaxone	0/7	(0)
Ciprofloxacin	25/25	(100)
Ofloxacin	26/26	(100)
Gentamicin	25/26	(96)
Tobramycin	23/24	(96)
Amikacin	24/26	(92)

bacter lwoffii bacteremia [5–8, 19, 20]. This study reviewed the cases of 18 patients with documented *Acinetobacter lwoffii* bacteremia, including a subgroup of 13 patients with an immunocompromised status, a condition that has not yet been reported in the literature. We found no difference in prevalence with regard to age or gender, and all of the patients except one had indwelling catheters. These findings imply that the host's immune status and the presence of an indwelling catheter are risk factors for *Acinetobacter lwoffii* bacteremia, as has been previously reported [5].

The types of catheters used in our patients included CIVC (76%), PIVC (18%) and PTCDC (6%). The patients with PIVCs had a shorter duration between catheter implantation and the bacteremic episode than the patients with CIVCs. The frequent contact of PIVCs with the body surface may have contributed to the early onset of bacteremia. Five patients in our study had community-acquired bacteremia. The portal of entry of these bacteremic episodes was difficult to determine. We speculated that the infections of the patients with CIVCs (patients 3, 5 and 17) who developed community-acquired infection might have been due to repeated manipulation of the CIVC outlet, resulting in a defect in the skin barrier or an increased incidence of contamination by the hands of self-care personnel. Primary *Acinetobacter lwoffii* bacteremia has not been reported. Patient 1 had chronic obstructive pulmonary disease manifesting as frequent wheezing attacks; he had taken low-dose prednisolone for symptomatic relief for at least 1 year. Steroid-induced skin atrophy and impaired immune status may have played a role in the development of infection in this patient. In bacteremic patients with autoimmune disease who are undergoing long-term steroid therapy, it is mandatory to perform further observational studies to determine whether the development of primary bacteremia has resulted from a defective skin barrier as a portal of entry.

It is generally accepted that removal of the catheter is the treatment of choice in catheter-related bacteremia [4]. However, the findings of this study indicate that removal of the catheter was not always necessary when appropriate antimicrobial therapy was given. The outcomes of the 18 patients in this series included one death that was attributable to the bacteremic event; all other patients recovered from their episodes. Patient 10 died 1 day after the onset of bacteremia because of his poor general condition with decompensated left ventricular function, acute renal failure and acute hypoxemic respiratory failure. All of the immunocompromised patients who received appropriate antibiotic therapy alone (patients 5, 12, 13, 15 and 18) recovered after their bacteremic episodes. The low virulence of *Acinetobacter lwoffii* may explain the good prognosis in these patients when treated with appropriate antibiotics, as suggested previously in the literature [5, 6, 19]. The time until defervescence was inversely related to removal of the catheter. The persistence of indwelling catheters gives microorganisms an opportunity to colonize and form a biofilm that can defeat bactericidal activity. The recovery of all patients in this series who were treated with antibiotics alone suggests that the existence of indwelling catheters is essential to the development of bacteremia, but it is not the sole factor in determining the outcome of *Acinetobacter lwoffii* bacteremia. The antibiograms of the 26 blood isolates showed high susceptibility to aminoglycosides, penicillin derivatives and quinolones but low susceptibility to third-generation cephalosporins. The spectrum of drug susceptibility was the same for patients with community-acquired bacteremia and those with hospital-acquired bacteremia, suggesting that the etiology of this condition was not related to prior exposure to antibiotics, although this inference needs to be further clarified.

In summary, this series of patients with *Acinetobacter lwoffii* bacteremia, most of whom were immunocompromised hosts and had indwelling catheters, shows that clinical syndromes resolved after appropriate antibiotic treatment and/or removal of the catheter. These data suggest that *Acinetobacter lwoffii* bacteremia appears to be associated with a low risk of mortality, even in immunocompromised hosts.

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