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Original Article

Approach of Empirical Antibiotic Treatment: Analyzing Bacterial Resistance of Community-acquired Bacteremia

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BACKGROUND/PURPOSE: Nosocomial bacterial resistance has been advanced and well studied in Taiwan, but there were few reports describing the antibiotic susceptibility of community-acquired pathogens. Through collecting data from those who received blood cultures in emergency department, we presented an epidemiological study to analyze appropriate empirical therapy for the community-acquired bacteremia in Southern Taiwan.

METHODS: From July 1998 to June 1999, patients presented at emergency department of Kaohsiung Veterans General Hospital with fever, chills or symptoms of sepsis were routinely performed two sets of blood cultures. Those of positive blood cultures without prior admission history to the hospital within 2 weeks were further analyzed for the etiologic pathogens, antibiotic susceptibility, and risk factors of community-acquired bacteremia.

RESULTS: A total of 303 episodes were enrolled for analysis, *Escherichia coli, Klebsiella pneumoniae,* and *Staphylococcus aureus* accounted for 76.3% of the isolates. Most of the community-acquired bacteremia was secondary bacteremia. Eighty-four percents of *E. coli,* 89% of *K. pneumoniae,* and 76% of *S. aureus* were susceptible to cefazolin. Susceptible rates of the three major pathogens to gentamicin were 72%, 92%, and 68% respectively.

CONCLUSION: While treating community-acquired bacteremia in Southern Taiwan, the first generation antibiotic, cefazolin plus gentamicin, was effective *in vitro* for the majority of cases. However, since the community-acquired bacteremia is mostly secondary in origin, it is necessary to explore the underlying primary lesions to attain therapeutic success. Further on-going epidemiological surveillance on bacterial resistance of community-acquired bacteremia is necessary to provide evidence-based appropriateness of empirical therapy.

KEY WORDS: antibiotic susceptibility, community-acquired bacteremia, empirical therapy

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Introduction

Antibiotic-resistant organisms causing nosocomial infection have emerged worldwide in recent decades, including Taiwan.[1–6] However, data regarding the antibiotic susceptibility of community-acquired pathogens is lacking, and empirical antibiotic therapy for sepsis is still controversial in Taiwan. Therefore, we conducted a prospective study of the period from July 1998 to June 1999 to investigate the epidemiological data on the bacterial resistance of causing community-acquired bacteremia in patients treated at the Veterans General Hospital in Kaohsiung, a tertiary medical center with 1,100 beds located in Southern Taiwan. The emergency department in this hospital receives around 140–180 cases per day, including patients with fever and sepsis.

Materials and Methods

Two sets of blood cultures were routinely performed on patients presenting with fever, chills, and/or signs of sepsis, and those with positive blood culture results were included in the study. Those patients with only one set of blood cultures positive for coagulase-negative staphylococcus were excluded. Patients that had been admitted to any hospital within the 2 weeks prior to presenting at the emergency department of the Veterans General Hospital in Kaohsiung were also excluded.

The antimicrobial susceptibility of the clinical isolates was determined by minimal inhibitory concentration using the MicroScan system. The antibiotics tested included ampicillin, amoxicillin/clavulanate, cefazolin, cephalothin, cefuroxime, ceftazidime, piperacillin, ciprofloxacin, imipenem, amikacin, gentamicin, sulfamethoxazole/trimethoprim, tetracycline, chloramphenicol, vancomycin, and rifampicin.

Results

After excluding seven cases due to contamination, a total of 303 cases of community-acquired bacteremia were enrolled. *Escherichia coli* ($n=140$, 46.2%), *Klebsiella pneumoniae* ($n=66$, 21.8%), and *Staphylococcus aureus* ($n=25$, 8.3%) constituted the three major pathogens, and accounted for 76.3% of the isolates (Table 1). For *E. coli*, 84% of cases were susceptible to cefazolin and 72% to gentamicin. For *K. pneumoniae*, 89% of cases were susceptible to cefazolin and 92% to gentamicin. For *S. aureus*, 76% of cases were susceptible to cefazolin and 76% to oxacillin (Tables 2 and 3). For Gram-negative isolates, the susceptibility rates to cefuroxime, amoxicillin/clavulanate, amikacin, aztreonam, ceftazidime, ciprofloxacin, and imipenem/cilastatin were over 80% for both *E. coli* and *K. pneumoniae*. Piperacillin was active against 31% of *E. coli* and 58% of *K. pneumoniae* infections. For Gram-positive strains, susceptibility rates to clindamycin were 68% for *S. aureus* and 100% for *Streptococcus* spp. Ciprofloxacin was active against 72% of *S. aureus*, 100% of *Streptococcus* spp., and 80% of *Enterococcus* spp. Vancomycin was active against 100% of *S. aureus*, *Streptococcus* spp., and *Enterococcus* spp.

Discussion

In our study, most of the community-acquired infections were secondary to an underlying focus in patients with certain predisposing factors, or underlying diseases. Urinary tract infections related to urolithiasis, benign prostatic hypertrophy, and urinary catheterization were caused by *E. coli* infection, which was the leading cause of bacteremia. Liver cirrhosis, biliary tract stones, and diabetes

Table 1. Distribution of pathogens causing community-acquired bacteremia ($n=303$)

Isolates	*n* (%)
Escherichia coli	140 (46.2)
Klebsiella pneumoniae	66 (21.8)
Staphylococcus aureus	25 (8.3)
Streptococcus spp.	12 (4.0)
Pseudomonas aeruginosa	11 (3.6)
Enterococcus spp.	9 (3.0)
Proteus mirabilis	8 (2.6)
Aeromonas hydrophila	8 (2.6)
Acinetobacter baumannii	6 (2.0)
Morganella morganii	5 (1.7)
Salmonella spp.	4 (1.3)
Enterobacter cloacae	4 (1.3)
Pasteurella multocida	2 (0.7)
Acinetobacter spp.	1 (0.3)
Moraxella osloensis	1 (0.3)
Pseudomonas alcaligenes	1 (0.3)

mellitus were the major predisposing factors for abdominal and biliary sepsis, which was the second most common cause of bacteremia. Diabetic patients with primary *K. pneumoniae*-infected liver abscesses and secondary bacteremia are very unique in Taiwan.[7,8] Therefore, exploration of the underlying primary lesions using imaging studies such as ultrasonography is required.

The definition of community-acquired bacteremia in the literature varies, which may have an influence on which strains are included in the various studies.[2] As some of the strains that we isolated were from patients with a history of admission to an intensive care unit more than 2 weeks prior to visiting the emergency department, they may have been the reason for the isolation of multi-drug resistant strains such as *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Enterobacter cloacae*. This suggests a need to revise the inclusion criteria, because these patients might have been colonized by nosocomial strains even though they had been discharged from hospitals, or chronic care facilities, for more than 14 days.[9]

Based on the epidemiological data available for Southern Taiwan, the three major pathogens appear to be

Table 2. The susceptibility rates of community-acquired Gram-negative bacteremia strains to antibiotics (Veterans General Hospital in Kaohsiung, 1999)

Antibiotics / Gram-negative strains	Susceptibility rate													
	CZ	CF	GM	AMP	SMX/TMP	C	CXM	AMC	AN	AZT	CAZ	IMP	PIP	CIP
Escherichia coli	84	20	72	26	43	53	86	82	96	96	96	96	31	95
Klebsiella pneumoniae	89	88	92	12	77	82	95	91	98	97	95	98	58	95
Pseudomonas aeruginosa	0	0	64	0	9	0	0	9	91	82	73	100	73	91
Proteus mirabilis	63	63	50	38	25	38	100	75	75	63	75	100	38	63
Aeromonas spp.	37.5	37.5	87.5	12.5	88	88	62.5	25	100	50	75	100	50	100
Acinetobacter baumannii	0	0	50	–	33	0	0	67	67	0	67	83	33	67
Morganella morganii	0	0	0	0	0	0	0	0	80	100	100	100	0	60
Salmonella spp.	–	–	–	50	75	25	–	75	–	–	75	75	–	75
Enterobacter cloacae	0	0	75	0	75	75	50	0	100	75	75	100	75	100
Pasteurella multocida	100	100	100	0	100	0	100	100	–	–	–	100	0	100
Acinetobacter spp.	0	0	100	–	100	100	100	100	–	–	–	100	100	100
Moraxella osloensis	100	100	100	–	100	100	100	100	–	–	–	100	100	100
Pseudomonas alcaligenes	0	0	100	–	0	0	0	100	–	–	–	100	100	100

CZ = cefazolin; CF = cephalothin; GM = gentamicin; AMP = ampicillin; SMX/TMP = sulfamethoxazole/trimethoprim; C = chloramphenicol; CXM = cefuroxime; AMC = amoxicillin/clavulanate; AN = amikacin; AZT = aztreonam; CAZ = ceftazidime; IMP = imipenem; PIP = piperacillin; CIP = ciprofloxacin.

Table 3. The susceptibility rates of community-acquired Gram-positive bacteremia strains to antibiotics (Veterans General Hospital in Kaohsiung, 1999)

Antibiotics / Gram-positive strains	Susceptibility rate											
	PCN	AMP	CZ	TC	OXA	E	SMX/TMP	CC	RIF	CIP	IMP	VAN
Staphylococcus aureus	4	4	76	60	76	60	80	68	92	72	76	100
Streptococcus spp.[a]	100	100	100	–	100	100	100	100	100	100	100	100
Enterococcus spp.	40	40	–	–	–	20	–	–	20	80	40	100

[a]including *Strep. bovis, Strep.* Gr A, B, and G. PCN=penicillin; AMP=ampicillin; CZ=cefazolin; TC=tetracycline; OXA=oxacillin; E=erythromycin; SMX/TMP=sulfamethoxazole/trimethoprim; CC=clindamycin; RIF=rifampicin; CIP=ciprofloxacin; IMP=imipenem; VAN=Vancomycin.

E. coli, *K. pneumoniae*, and *S. aureus*. This strongly suggests that therapy for patients with community-acquired bacteremia should focus on these three pathogens, and a combination of cefazolin and gentamicin seems to be an appropriate treatment, although oxacillin could be used to treat Gram-positive bacteremia. For patients with more critical conditions, such as severe sepsis, it might be cost-effective to use cefuroxime or amoxicillin/clavulanate for probable Gram-negative bacteremia, and vancomycin for suspected Gram-positive bacteremia. Piperacillin was not an adequate treatment for community-acquired bacteremia due to its low susceptibility rate. Though aztreonam, ceftazidime, imipenem/cilastatin, and ciprofloxacin showed good activity *in vitro*, they are expensive and should be reserved for nosocomial infections.

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