Clinical and Microbiological Characteristics of Community-Acquired *Staphylococcus lugdunensis* Infections in Southern Taiwan[†]

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Most *Staphylococcus lugdunensis* strains (49/59, 83%) were related to clinical infections, were susceptible to most antimicrobial agents with an overall oxacillin-resistant rate of 5% (3/58), and carried relatively great genetic diversity. Community-acquired infections (41/49, 84%) were dominant, often developed in patients with comorbidity, and had rather benign clinical courses without mortality.

Staphylococcus lugdunensis, a member of coagulase-negative staphylococci (CoNS) first described in 1988 by Freney et al. (5a), often causes skin and soft tissue infections; severe infections attributed to this organism are not rare (1, 8). Its clinical course and microbiological characteristics may resemble those of the coagulase-positive *Staphylococcus aureus* (4, 6) and has been associated with more invasive infections (2, 4, 8, 11, 13). The purpose of this study was to investigate the clinical and microbiological characteristics of *S. lugdunensis* isolates at a tertiary hospital in southern Taiwan.

A total of 59 *S. lugdunensis* isolates from 57 patients were collected at National Cheng Kung University Hospital between August 2005 and September 2009. CoNS was identified by conventional methods and the GP card Vitek 2 (bioMérieux, Marcy l'Etoile, France). The further confirmation was carried out using 16S rRNA sequencing. *S. lugdunensis* isolates that were the only or predominant pathogen from wound or pus culture or derived from sterile body fluid or bloodstream were included for analysis.

Oxacillin and cefoxitin susceptibilities were tested by the MIC dilution method. Cefoxitin and other antimicrobial susceptibilities were evaluated by the disk diffusion method (3). *S. aureus* ATCC 25923 and ATCC 29213 were used as quality control strains. Pulsed-field gel electrophoresis (PFGE) of SmaI-digested genomic DNA samples of *S. lugdunensis* isolates was carried out with a CHEF Mapper XA apparatus (Bio-Rad Laboratories, Hercules, CA), according to the instruction manual. PFGE patterns were interpreted in accordance with the criteria of Tenover et al. (14). *S. lugdunensis* strains were an-

alyzed for staphylococcal cassette chromosome *mec* element (SCC*mec*) typing and amplification of the *mecA* and 16S rRNA genes by multiplex PCR and traditional PCR, respectively (10, 15). The purified PCR products were directly sequenced using the automated ABI Prism 3730 DNA sequencer (Applied Biosystems, Foster, CA).

A total of 49 of 59 *S. lugdunensis* strains (83%) derived from 48 patients were related to clinically significant infections. Diabetes mellitus (11/48, 23%), malignancy (6/48, 13%), and end-stage renal disease (5/48, 10%) were the most common comorbidities. The majority of *S. lugdunensis* infections (41/49, 84%) were community acquired. Skin and soft tissue infection (44/49, 90%) was the major type of clinical presentation. All three bacteremia episodes were catheter related and developed in the intensive care unit. None of the three patients had clinical features of infective endocarditis. Transthoracic echocardiography was not performed in any case. Two patients

TABLE 1. Antimicrobial susceptibility tests for 58 *S. lugdunensis* isolates

Antibiotic	No. (%) of sensitive isolates			P value ^a
	Community acquired (n = 46)	Nosocomial (n = 12)	Total (n = 58)	
Penicillin	24 (52)	3 (25)	27 (47)	0.1148
Oxacillin	46 (100)	11 (92)	57 (98)	0.2069
Cefoxitin	46 (100)	10 (83)	56 (97)	0.0399
Clindamycin	35 (76)	8 (67)	43 (77)	0.4865
Gentamicin	46 (100)	8 (67)	54 (93)	0.0012
Co-trimoxazole	45 (98)	11 (92)	56 (97)	0.3739
Erythromycin	32 (70)	7 (58)	39 (67)	0.5023
Levofloxacin	46 (100)	12 (100)	58 (100)	
Moxifloxacin	45 (98)	12 (100)	57 (98)	
Vancomycin	46 (100)	12 (100)	58 (100)	
Teicoplanin	46 (100)	12 (100)	58 (100)	

^a Community-acquired group versus nosocomial group, examined by Fisher's exact test (two tailed).

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FIG. 1. Genetic relationships and SmaI pulsed-field gel electrophoresis (PFGE) patterns of 49 *S. lugdunensis* isolates from 48 patients. PFGE groups are designated A to P; B, E, F, I, J, K, M, O, and P denote unclustered isolates. R denotes oxacillin resistance, S denotes isolates from skin and soft tissue infection, T denotes isolates from catheter-related infection, U denotes isolates from urinary tract infection, and X denotes isolates from bacteremia.

showed improvement soon after catheter removal and antimicrobial therapy, and one patient died 9 days after catheter-related bacteremia even treated with vancomycin. *S. lugdunensis* was cultured as the only pathogen in 32 specimens (65%). *S. lugdunensis* was the predominant pathogen in 17 specimens (16 patients) with polymicrobial infections or colonization. The most common coisolate identified was another CoNS isolate (8 patients), and the others included oxacillin-resistant *Staphylococcus aureus*, group B streptococci, group D streptococci, *Peptostreptococcus* species, *Bacteroides fragilis*, *Enterococcus* species, Gram-positive bacilli, micrococci, and *Stenotrophomonas maltophilia*. These coisolates did not influence the treatment or clinical course. All the community-acquired *S. lugdunensis* infections had rather benign clinical courses without mortality. The results of the antimicrobial susceptibility test are shown in Table 1. The oxacillin MICs for 57 of 58 strains (98%) of *S. lugdunensis* were ≤ 2 $\mu\text{g/ml}$, and cefoxitin MICs for 56 of 58 strains (97%) were ≤ 4 $\mu\text{g/ml}$. The overall oxacillin-resistant rate was 5% (3 in 58), according to the recommendations of the CLSI in 2010 (3). All three oxacillin-resistant *S. lugdunensis* isolates had the *mecA* gene and were derived from nosocomial infections. The genetic relationships and SmaI PFGE patterns of 49 *S. lugdunensis* infection isolates are shown in Fig. 1. Sixteen pulsotypes were identified from 49 isolates. The following two major PFGE pulsotypes accounted for 25 (51%) of the 49 isolates: pulsotype C (18 isolates) and pulsotype L (7 isolates). Nine did not cluster with any other isolates.

Community-acquired *S. lugdunensis* bacteremia is associated with endocarditis in up to 50% of patients and could be fatal (2, 4). Böcher et al. (1) reported that *S. lugdunensis* is isolated from 13% of 159 abscesses from general practice during a 6-month period. Recurrent and invasive *S. lugdunensis* infections were seen in 7 (1.4%) and 14 (2.9%) of 491 patients in 4 years (1). Our study revealed that the major isolates of *S. lugdunensis* infections were derived from community-acquired infections with common comorbidity of diabetes mellitus, malignancy, and end-stage renal disease. These results are different from the results reported by Kleiner et al. showing that the major comorbidity of *S. lugdunensis* infections was related to surgery or recent trauma (47%) (7). Skin and soft tissue infection was the most common type of infection. Only one death occurred, the patient with nosocomial catheter-related bacteremia. Sixteen pulsotypes identified from our 49 *S. lugdunensis* isolates indicated relatively great genetic diversity among our clinical strains related mainly to community-acquired infections. However, pulsotype C containing 18 isolates and pulsotype L containing 7 isolates suggest the possibility of transmission of *S. lugdunensis* from human to human.

S. lugdunensis is classified as a CoNS species in the routine microbiological laboratory. If a positive culture result for *S. lugdunensis* is reported, the clinical significance other than contamination should be considered seriously. In addition to the clinical presentation and course resembling those of *S. aureus*, *S. lugdunensis* shares the same CLSI antimicrobial susceptibility and resistance breakpoints with *S. aureus*. There are higher oxacillin MIC values in susceptibility and resistance for treatment of *S. lugdunensis* than those for treatment of other CoNS (MIC of ≤ 2 and MIC of ≥ 4 $\mu\text{g/ml}$ versus MIC of ≤ 0.25 $\mu\text{g/ml}$ and MIC of ≥ 0.5 $\mu\text{g/ml}$, respectively) (3). In our clinical

infection isolates, oxacillin-susceptible strains decrease to 4 of 49 (8.2%) if *S. lugdunensis* is not identified from the CoNS species. Delayed or incorrect diagnosis of *S. lugdunensis* infections may result in misidentified antimicrobial resistance and overuse of more powerful second-line antibiotics for treatment.

S. lugdunensis, unlike other CoNS species, has high susceptibility to most antibiotics (5). The overall oxacillin-resistant rate was 5% (3/58), which was similar to that in previous reports (12). All three oxacillin-resistant *S. lugdunensis* isolates had the *mecA* gene in this study, in contrast to other reports that most oxacillin-resistant *S. lugdunensis* strains lacked the *mecA* gene (9, 13). For the three *mecA* gene-positive isolates in this study, one had an oxacillin MIC of ≥ 4 $\mu\text{g/ml}$, and two had MICs of 2 $\mu\text{g/ml}$; two had cefoxitin MICs of ≥ 8 $\mu\text{g/ml}$, and one had a MIC of 4 $\mu\text{g/ml}$. Current MIC breakpoints for oxacillin or cefoxitin recommended by the CLSI could not predict the presence of the *mecA* gene. Our data revealed a zone diameter for cefoxitin of ≤ 22 mm, which correlated with the presence of the *mecA* gene.

In summary, *S. lugdunensis* has emerged as an important organism in both community-acquired and nosocomial infections. The majority of *S. lugdunensis* strains in our study were clinically significant, derived mainly from community-acquired infections in patients with comorbidity of diabetes mellitus, malignancy, and end-stage renal disease. They were susceptible to most antimicrobial agents and carried relatively great genetic diversity. Community-acquired *S. lugdunensis* infections had rather benign clinical courses without mortality.

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