Clinical and Microbiological Characteristics of Community-Acquired

*Staphylococcus lugdunensis* Infections in Southern Taiwan

An-Bang Wu,¹ Ming-Cheng Wang,¹,² Chin-Chung Tseng,¹ Wei-Hung Lin,³ Ching-Hao Teng,⁴ Ay-Huey Huang,⁵ Kuei-Hsiang Hung,⁶ Chuan Chiang-Ni,⁶ and Jiunn-Jong Wu⁶,⁷ *

¹Division of Nephrology, Department of Internal Medicine, National Cheng Kung University Hospital, Tainan, Taiwan

²Institute of Clinical Pharmacy, College of Medicine, National Cheng Kung University, Tainan, Taiwan

³Institute of Clinical Medicine; College of Medicine, National Cheng Kung University, Tainan, Taiwan

⁴Institute of Molecular Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan

⁵Department of Pathology, National Cheng Kung University Hospital, Tainan, Taiwan

⁶Department of Medical Laboratory Science and Biotechnology, College of Medicine, National Cheng Kung University, Tainan, Taiwan

⁷Infectious Disease and Signaling Research Center, National Cheng Kung University, Tainan, Taiwan

*Corresponding author. Mailing address: Department of Medical Laboratory Science and Biotechnology, College of Medicine, National Cheng Kung University, No. 1 University Road, Tainan 70101, Taiwan. Phone: 886-6-2353535, ext 5775. Fax: 886-6-2363956. E-mail: jjwu@mail.ncku.edu.tw.*
Most *Staphylococcus lugdunensis* strains (49/59, 83%) were related to clinical infections, susceptible to most antimicrobial agents with overall oxacillin resistant rate of 6% (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.

**Keywords:** coagulase-negative staphylococcus, *Staphylococcus lugdunensis*, community-acquired infection, antimicrobial resistance, mecA gene, pulsed-field gel electrophoresis.
Staphylococcus lugdunensis, a member of CoNS first described in 1988 by Freney et al, 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 the conventional methods and the GP card Vitek 2 (bioMérieux, Marcy l'Etoile, France). The further confirmation was carried out using the 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 minimum inhibitory concentration (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 analyzed for SCCmec 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).

Forty-nine 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 showed improvement soon after catheter removal and antimicrobial therapy, one patient died nine 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 co-isolates identified was another CoNS (8 patients), 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 co-isolates 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 antimicrobial susceptibility test are shown in Table 1. The oxacillin MICs for 57 of 58 (98%) strains of *S. lugdunensis* were ≤ 2 µg/ml, cefoxitin MICs for 56 of 58 strains (97%) were ≤ 4 µg/ml; the overall oxacillin resistant rate was 5% (3 in 58) according to the recommendations of CLSI 2010. All the three oxacillin-resistant *S. lugdunensis* isolates had mecA gene and were derived from nosocomial infections. Genetic relationships and Smal PFGE patterns of 49 *S. lugdunensis* infection isolates are shown in Figure 1. Sixteen pulsotypes were identified from 49 isolates. 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). Bärcher et al. 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 the community-acquired infections with common comorbidity of diabetes mellitus, malignancy, and end-stage renal disease. It is different from the results reported by Kleiner et al. 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 in 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 mainly related 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 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 ≤ 2 and MIC ≥ 4 µg/ml versus MIC ≤ 0.25 µg/ml and MIC ≥  
0.5 µg/ml, respectively) (3). In our clinical infection isolates, oxacillin-susceptible strains  
will decrease to 4 of 49 (8.2 %) if *S. lugdunensis* was 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 6% (3/58), which was similar to the 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 oxacillin MIC $\geq 4 \mu g/ml$ and two had MICs of $2 \mu g/ml$; two had cefoxitin MIC $\geq 8 \mu g/ml$ and one had MIC of $4 \mu g/ml$. Current MIC breakpoints for oxacillin or cefoxitin recommended by CLSI could not predict the presence of the *mecA* gene. Our data revealed a zone diameter for cefoxitin $\leq 22$ mm 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, mainly derived 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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REFERENCES


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

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Sensitive No (%)</th>
<th>Community-acquired isolates (n = 46)</th>
<th>Nosocomial isolates (n = 12)</th>
<th>Total isolates (n = 58)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>24 (52)</td>
<td>3 (25)</td>
<td>27 (47)</td>
<td>0.1148</td>
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<tr>
<td>Oxacillin</td>
<td>46 (100)</td>
<td>11 (92)</td>
<td>57 (98)</td>
<td>0.2069</td>
<td></td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>46 (100)</td>
<td>10 (83)</td>
<td>56 (97)</td>
<td>0.0399</td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>35 (76)</td>
<td>8 (67)</td>
<td>43 (77)</td>
<td>0.4865</td>
<td></td>
</tr>
<tr>
<td>Gentamicin</td>
<td>46 (100)</td>
<td>8 (67)</td>
<td>54 (93)</td>
<td>0.0012</td>
<td></td>
</tr>
<tr>
<td>Co-trimoxazole</td>
<td>45 (98)</td>
<td>11 (92)</td>
<td>56 (97)</td>
<td>0.3739</td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>32 (70)</td>
<td>7 (58)</td>
<td>39 (67)</td>
<td>0.5023</td>
<td></td>
</tr>
<tr>
<td>Levofoxacin</td>
<td>46 (100)</td>
<td>12 (100)</td>
<td>58 (100)</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>45 (98)</td>
<td>12 (100)</td>
<td>57 (98)</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Vancomycin</td>
<td>46 (100)</td>
<td>12 (100)</td>
<td>58 (100)</td>
<td>—</td>
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</tr>
<tr>
<td>Teicoplanin</td>
<td>46 (100)</td>
<td>12 (100)</td>
<td>58 (100)</td>
<td>—</td>
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</tr>
</tbody>
</table>

* Community-acquired versus nosocomial groups, examined by Fisher’s exact test (2-tail).
Figure legends

Figure 1. Genetic relationships and SmaI pulsed-field gel electrophoresis (PFGE) patterns of 49 S. lugdunensis isolates from 48 patients. PFGE groups are designated A-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; X denotes isolates from bacteremia.