Incidence, Characteristics, and Outcomes of *Staphylococcus lugdunensis* Bacteremia[▽]

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Of 63 patients with *Staphylococcus lugdunensis* bacteremia, 15 (23.8%) had clinically significant bacteremia, with an incidence of 1.3 cases per 100,000 admissions. Of the five patients with community-acquired *S. lugdunensis* bacteremia, three had endocarditis. Catheters were the most common portal of entry for health-care-associated or hospital-acquired bacteremia. Only one patient died of bacteremia-related causes.

Since the first isolation of *Staphylococcus lugdunensis* in 1988 (6), this coagulase-negative staphylococcus (CoNS) has emerged as an important human pathogen (5). *S. lugdunensis* behaves more like *Staphylococcus aureus* than do other CoNS, causing more invasive infections such as infective endocarditis (4, 5, 12). Endocarditis caused by *S. lugdunensis* has been notorious for the aggressive destruction of native valves and life-threatening complications (5). Although *S. lugdunensis* bacteremia (SLB) has been known to be associated with fatal endocarditis, the incidence and clinical significance of SLB are largely unknown, with only a few small case studies (4, 12). To evaluate the incidence, characteristics, and outcomes of SLB, we reviewed the data for all patients with SLB from the available computerized database of seven general hospitals throughout the Republic of Korea between January 1999 and May 2009.

SLB was considered as clinically significant if ≥ 2 separate blood cultures or one blood culture and another sterile culture were positive and if systemic inflammatory response syndrome (SIRS) was present without any alternate explanation. Bacteremia was classified as community acquired, health care associated, or hospital acquired, as described elsewhere (7). SIRS, severe sepsis, and septic shock were defined as described elsewhere (2). Clinical isolates were identified using MicroScan Gram-positive combo panels (Dade Behring, West Sacra-

mento, CA) or Vitek 2 cards for Gram-positive cocci (bioMérieux, Marcy l'Etoile, France). Antimicrobial susceptibilities were determined by automated systems using standard criteria (3).

Of the 1,117,598 admissions to the seven study hospitals during the study period, a total of 63 patients were diagnosed with SLB, yielding an incidence of 5.6 patients per 100,000 admissions. The median proportions of *S. lugdunensis* among all blood isolates and all CoNS blood isolates were 0.26% (range, 0.12 to 1.21%) and 0.9% (range, 0.55 to 3.4%), respectively. Of the 63 patients with SLB, 15 were considered to have clinically significant SLB, making the incidence of clinically significant SLB 1.3 patients per 100,000 admissions.

The clinical characteristics of the 15 patients with significant SLB are shown in Table 1. Their median age was 55 years, and nine (60.0%) were females. Fourteen were adults, and the other was a child 10 years old. Diabetes was the most common underlying illness (5/15; 33.3%), followed by hematological malignancy (3/15; 20.0%). Five patients each (33.3%) had community-acquired, health-care-associated, and hospital-acquired bacteremia. The source of bacteremia was unknown in eight patients (53.3%), a central venous catheter in five (33.3%), a continuous ambulatory peritoneal dialysis (CAPD) catheter in one (6.7%), and cellulitis in one (6.7%). Of the 10 patients with health-care-associated or hospital-acquired bacteremia, 6 (60%) had catheters as the source of bacteremia. In contrast, four of the five patients (80%) with community-acquired bacteremia had unknown sources.

Four patients (26.7%) had endocarditis, with two of these having underlying valvular heart diseases. Three of these patients had community-acquired bacteremia, and one had

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TABLE 1. Characteristics of 15 patients with clinically significant *S. lugdunensis* bacteremia

Sex, age (yr)	Acquisition	Underlying disease(s)	No. of positive/total culture bottles, other positive cultures	Portal of entry	Presence of endocarditis, site of involvement	Surgery	Antibiotic therapy (duration in days)	Outcome
Female, 21	Community acquired	Congenital aortic stenosis	2/3	Unknown	Present, aortic/mitral/tricuspid valves, popliteal artery	Replacement of aortic/mitral valves, endarterectomy	Vancomycin and gentamicin (25), cefazolin (29)	Recovered
Male, 55	Health care associated	Liver transplantation, aortic stenosis with bicuspid aortic valve	3/3	Unknown	Present, aortic valves, aorta wall	Replacement of aortic valves/ascending aorta (Bentall operation)	Vancomycin and meropenem (6), vancomycin (18)	Death, surgical site bleeding
Male, 38	Community acquired	None	4/4	Unknown	Present, mitral valves, femoral artery	Replacement of mitral valves, femoral artery embolectomy	Cefazolin (40)	Recovered
Male, 83	Community acquired	None	4/6	Unknown	Present, mitral valves	Not done	Ceftriaxone and gentamicin (3)	Unknown
Male, 51	Hospital acquired	Stomach cancer	3/3	Unknown	Absent	Not done	Ceftriaxone (3)	Unknown
Female, 48	Hospital acquired	Lymphoma, diabetes	3/3	CVC ^a	Absent	Not done	Ciprofloxacin (6), vancomycin (15)	Recovered
Female, 21	Health care associated	Multiple myeloma	3/3, catheter	CVC	Absent	Not done	Vancomycin (15)	Recovered
Male, 60	Hospital acquired	Amorphous lateral sclerosis	2/2	CVC	Absent	Not done	Piperacillin-tazobactam (14), teicoplanin (7)	Recovered
Female, 70	Hospital acquired	Diabetes, Cushing's syndrome, hypothyroidism	2/2	Unknown	Absent	Not done	Ampicillin-subactam (18), teicoplanin (16)	Death, <i>Klebsiella pneumoniae</i> bacteremia
Male, 76	Community acquired	Generalized pustular psoriasis	3/3	Cellulitis	Absent	Not done	Cefazolin (14)	Recovered
Female, 50	Health care associated	Multiple myeloma	3/3	CVC	Absent	Not done	Piperacillin-tazobactam and ciprofloxacin (21), vancomycin (20)	Recovered
Female, 10	Hospital acquired	Cirrhillemia	2/2	CVC	Absent	Not done	Ampicillin-subactam (2), vancomycin (7)	Recovered
Female, 71	Community acquired	Diabetes	2/2	Unknown	Absent	Not done	Levofloxacin (2), piperacillin-tazobactam (10)	Recovered
Female, 82	Health care associated	Subdural hematoma, diabetes	2/2	Unknown	Absent	Not done	Ceftriaxone (5), meropenem (10)	Recovered
Female, 65	Health care associated	Diabetes, cerebral infarction, renal failure	1/2, ascites	CAPD ^b catheter (peritonitis)	Absent	Not done	Vancomycin and ceftazidime (9)	Death, SLB ^c related

^a CVC, central venous catheter.^b CAPD, continuous ambulatory peritoneal dialysis.^c SLB, *Staphylococcus lugdunensis* bacteremia.

health-care-associated bacteremia. Valve replacement surgery was successful in three of these four patients; the fourth was transferred to another hospital, and outcomes were not available.

Three of the 15 patients (20.0%) met the criteria for severe sepsis, and 1 (6.7%) met the criteria for septic shock. Of the 14 isolates evaluated, 12 (85.7%) were resistant to penicillin and 4 (28.6%) were resistant to oxacillin. In contrast, all isolates were susceptible to vancomycin and rifampin. Of the 13 evaluable patients, 3 (23.1%) died in the hospital, including 1 (7.7%) bacteremia-related death. In no case was a recurrence of SLB observed after the completion of antimicrobial therapy.

To our knowledge, this is the largest series of SLB patients to date. In comparison, one study in a single hospital found that 20 patients had SLB over a period of 12 years, whereas a second study in three hospitals reported 28 such patients over 5 to 10 years (4, 12). These reports, however, did not include the incidence of SLB. Two additional studies have reported that the frequencies of isolation of *S. lugdunensis* were 0.3% (4 of 1,256 CoNS blood isolates) and 0.7% (7 of 1,021 patients with CoNS bacteremia) (1, 10). We found that the incidence rate of SLB was 5.6 patients per 100,000 admissions, with a median proportion of *S. lugdunensis* among all CoNS blood isolates of 0.9%. These findings indicate that SLB occurs very rarely in clinical practice. Moreover, we found that only 23.8% (15/63) of patients with SLB had clinically significant SLB, a rate comparable with the 30% (6/20) rate previously reported (4) and with the proportions of significant bacteremia among patients with CoNS bacteremia (26.4%) (8) and among patients with non-*Staphylococcus epidermidis* CoNS bacteremia (20%) (11). These findings suggest that *S. lugdunensis* is a constituent of normal human skin flora that, like other CoNS, frequently contaminates blood cultures.

The frequency of endocarditis among patients with SLB has been largely unknown. Although one study of 28 patients with SLB found that all had significant bacteremia and nearly 50% had endocarditis (12), a second study found that only 1 of 6 patients with clinically significant SLB over 12 years had endocarditis (4), and a third study found that 0 of 7 patients with SLB over 10 years had endocarditis (1). In comparison, we found that 4 of 63 patients with SLB (6.3%) and 4 of 15 with significant SLB (26.7%) had endocarditis. These findings suggest that patients with significant SLB, especially community-acquired SLB, should be evaluated for the presence of endocarditis.

We found that central venous catheters were the most common portals of entry in patients with health-care-associated or hospital-acquired bacteremia. In comparison, other studies have reported that 5 of 6 patients with significant SLB had catheter-related bacteremia (3 hemodialysis catheters and 2 long-term venous catheters) (4) and that 11 of 15 patients with SLB but without endocarditis had catheter-related bacteremia, most nosocomially acquired (12). These findings suggest that like other CoNS, *S. lugdunensis* has pathogenic potential for foreign-device-related infections, in hospitals or health-care-related circumstances. A recent guideline for intravascular catheter-related infections commented on the importance of *S. lugdunensis* catheter-related infections (9). However, we did not observe an association between catheter-related SLB and endocarditis.

Unlike other CoNS, *S. lugdunensis* is susceptible to a wide array of antimicrobial agents (5). In contrast, 5 of 20 isolates (25.0%) were found to be resistant to multiple antimicrobials, including oxacillin (4). We found that the rates of antimicrobial resistances among isolates from patients with significant SLB were even higher, with 85.7% resistant to penicillin and 28.6% resistant to oxacillin. These unusually high rates of antimicrobial resistances may be due, at least in part, to the relatively low proportion of our patients with community-acquired SLB (33.3%) and the high rates of antimicrobial resistance in the Republic of Korea.

The mortality rates of patients with SLB have been reported to vary, especially regarding mortality related to the presence of endocarditis. For example, one study of 6 patients with SLB, including one with endocarditis, reported no deaths (4), whereas another found that 3 of 13 patients (23.1%) with endocarditis and 2 of 15 (13.3%) without endocarditis died (12). Due to the small numbers of patients with endocarditis and the two patients with unknown clinical outcomes, we could not evaluate differences in clinical outcomes related to the presence of endocarditis. There was only one bacteremia-related death among our patients (7.7%), which may have been related to the performance of valve surgeries in all of our patients with endocarditis. However, the in-hospital mortality rate among our patients was similar to that of another study (12), suggesting that deaths in patients with significant SLB may be due to the presence of serious underlying diseases.

In conclusion, we found that clinically significant SLB occurred very rarely in clinical practice. Patients with clinically significant SLB should be evaluated for the presence of endocarditis and catheter-related infections. SLB was associated with a low risk of bacteremia-related mortality.

All authors have no conflicts of interest.

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