JOURNAL OF CLINICAL MICROBIOLOGY, Feb. 2002, p. 654–656 Vol. 40, No. 2
0095-1137/02/$04.00+0 DOI: 10.1128/JCM.40.2.654–656.2002

Frequency of Isolation of *Staphylococcus lugdunensis* in Consecutive Urine Cultures and Relationship to Urinary Tract Infection

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Received 11 July 2001/Returned for modification 10 September 2001/Accepted 18 November 2001

Recent reports associate *Staphylococcus lugdunensis* with severe infection in humans. The frequency of this microorganism in urine cultures is unknown. Five hundred isolates of coagulase-negative staphylococci (CoNS) were recovered from 4,652 consecutive urine specimens submitted for culture to the Mayo Clinic Microbiology Laboratory. Thirty-one (6%) of 500 isolates of CoNS were identified as *S. lugdunensis*. In no case was *S. lugdunensis* isolated in pure culture; 29 (94%) of 31 *S. lugdunensis* isolates were part of mixed nonpathogenic flora. Medical records were reviewed for 30 of the 31 patients from whom these 31 isolates were isolated. Twenty-one (70%) of the 30 evaluable patients were not treated with antibiotics; the remaining 9 (30%) of 30 patients were treated with antibiotics that may be effective against *S. lugdunensis*. *S. lugdunensis* may be an unrecognized yet infrequent cause of urinary tract infection.

Staphylococcus lugdunensis is a member of the coagulase-negative staphylococci (CoNS) which has been associated with serious infections in humans. Patients infected with the organism have a clinical presentation much like that of patients infected with *Staphylococcus aureus*. Reports have associated *S. lugdunensis* with skin and soft tissue infections (3, 5), respiratory infections (3), bacteremia, including endocarditis (1, 2, 3, 6, 7, 8, 11), intravascular catheter or pacemaker infections (3), prosthetic joint infections (9), and peritonitis (10).

We are aware of only one study which has determined the frequency of *S. lugdunensis* in consecutive clinical cultures. Herchline and Ayers (3) surveyed *S. lugdunensis* isolates from clinical specimens in their laboratory over a 63-month period. They noted the following anatomical distribution frequencies for 229 *S. lugdunensis* isolates recovered from 155 specimens submitted from 143 patients: skin, $n = 7$ (4.5%); abscesses, $n = 14$ (9.0%); wounds, $n = 65$ (41.9%); respiratory tract, $n = 13$ (8.4%); blood, $n = 15$ (9.7%); intravascular catheters, $n = 11$ (7.7%); urogenital tract, $n = 15$ (9.7%); and other, $n = 15$ (9.7%) (3). Those investigators did not specify how many of the specimens from the urogenital site were urine specimens, and they did not indicate the reporting procedures for urine specimens. For example, it is not known whether *S. lugdunensis* isolates were identified in urine or whether these isolates occurred in pure culture or were part of a mixed flora, and the colony counts are not known.

The objectives of the present study were to determine the frequency of *S. lugdunensis* in 4,652 consecutive urine specimens submitted to our laboratory for bacterial culture and the relationship between these isolates and urinary tract infection.

Patient population. All urine specimens for culture were collected from patients evaluated at the Mayo Medical Center in Rochester, Minnesota, between 24 July 2000 and 12 September 2000. The study was reviewed and approved by the Mayo Clinic Institutional Review Board; samples from patients who declined use of their specimens and medical histories from evaluation were excluded from the study, according to Minnesota Statute 144.335 (Patient Consent to Release of Records). The Mayo Medical Center consists of two large teaching hospitals (combined number of beds, ~1,800) and a large subspecialty clinic. The urine specimens included those collected by spontaneous voiding or catheterization.

***S. lugdunensis* isolation.** All specimens were cultured on sheep blood (trypticase soy agar [TSA II] with 5% sheep blood; BBL) or eosin-methylene blue agar (Levine EMB; BBL). The plates were incubated overnight at 35°C in 5 to 7% CO_2. Technologists subcultured any colony that resembled CoNS. Gram staining was performed to confirm that the colonies were staphylococci. Isolates from subcultures were identified as *S. lugdunensis* if they hydrolyzed L-pyrrolidonyl-β-naphthylamide (PYR) and decarboxylated ornithine.

Patient record review. The medical records of patients with urine cultures positive for *S. lugdunensis* were reviewed for symptoms and signs of urinary tract infection (UTI). These signs and symptoms included dysuria, frequency, urgency, and costovertebral tenderness. Data on underlying medical disorders and antimicrobial treatment were also recorded. Telephone interviews were also conducted for patients who were treated with antibiotics but for whom there was no indication of their response in the medical record.

Five hundred isolates of CoNS were isolated from 4,652 urine specimens. Thirty-one (6%) of the 500 isolates of CoNS were identified as *S. lugdunensis*. Medical records were available for 30 of 31 patients from whom these isolates were cultured. These patients had no common underlying medical disorders. Nine of the 30 patients fulfilled at least one criterion for UTI (dysuria, frequency, urgency, or costovertebral tenderness). For 21 of the 30 patients, there was no documentation of symptoms or signs of UTI in the medical record.

Three of the 30 urine specimens positive for *S. lugdunensis* were collected via a catheter, and 1 of the 3 patients from

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whom samples were collected via a catheter fulfilled the criteria for having an UTI. Two of the three patients from whom specimens were collected via a catheter had urologic conditions that required a catheter. For the other eight patients who fulfilled the criteria for having an UTI, urine was collected midstream during voiding.

Twenty-nine (94%) of the 31 *S. lugdunensis* isolates occurred as part of unspecified mixed flora, 1 other unidentified organism was present (<10,000 CFU/ml) in 1 (3%) of the 31 patients, and *Pseudomonas aeruginosa* (10,000 to 100,000 CFU/ml) was detected in 1 (3%) of the 31 patients. Among the 30 patients from whom *S. lugdunensis* was isolated, 53% were women age 65 years or older (in contrast, isolates from women in this same age range accounted for 20% of the total isolates of CoNS recovered), 40% were females younger than age 65 years, 3% were men age 65 years or older, and 3% were males younger than age 65 years.

There were no positive blood cultures for the patients from whom the 500 isolates of CoNS were isolated. Among the 30 urine specimens positive for *S. lugdunensis*, 24 (80%) specimens were collected midstream during voiding and 3 (10%) specimens were collected via a catheter; the method of collection was not specified for 3 (10%) specimens. For isolates of CoNS overall, 78% were collected midstream and 18% were collected via a catheter; the method of collection was not specified for 4% of the specimens.

Twenty-one (70%) of the 30 evaluable patients with *S. lugdunensis*-positive urine cultures were not treated with antibiotics or their treatment was not specified in the medical record. As mentioned above, there was no indication from the medical record that any of these patients had signs and symptoms of an UTI or that they eventually developed symptoms and signs of an UTI. The remaining 9 (30%) of the 30 evaluable patients were treated with antibiotics that may be effective against *S. lugdunensis.* These antibiotics included trimethoprim-sulfamethoxazole, ciprofloxacin, and levofloxacin. Seven of these nine patients responded 3 to 14 days after initiation of treatment. Two of the nine antibiotic-treated patients did not respond to antibiotics; after further workup, one patient was diagnosed with uninhibited detrusor contractions and the second patient was diagnosed with pelvic discomfort, possibly related to a gastrointestinal etiology.

The results of our study suggest that *S. lugdunensis* may be an unrecognized yet infrequent cause of UTIs. *S. lugdunensis* accounted for 6% of isolates of CoNS recovered from cultures of urine in our study. We cannot be certain that *S. lugdunensis* was a definite uropathogen. However, among 9 of the 30 evaluable patients from whom *S. lugdunensis* was isolated from the urine and for whom antibiotics were provided, 7 patients responded. These antibiotics may well have been effective against *S. lugdunensis*.

Our current practice is to screen all isolates of CoNS from sterile body fluids other than urine and sterile body tissues for PYR hydrolysis and ornithine decarboxylate activity. Isolates of CoNS from these anatomical sources that are confirmed to be *S. lugdunensis* are screened for beta-lactamase activity (cefinase method) and the presence of the *mecA* gene. In our experience, beta-lactamase activity is present in some (~40%) *S. lugdunensis* isolates; however, to date we have not identified the *mecA* gene in any isolate of *S. lugdunensis* (P. C. Kohner, J. Uhl, and F. R. Cockerill, Abstr. 101st Gen. Meet. Am. Soc. Microbiol. 2001, abstr. C-91, p. 111, 2001). Herchline and colleagues reported that 24% of 59 *S. lugdunensis* isolates were positive for beta-lactamase (4). Therefore, most (~60%) *S. lugdunensis* isolates should be susceptible to ampicillin, as well as cephalosporins, which are commonly used to treat uncomplicated UTIs. We have also noticed in our practice that most isolates are susceptible to quinolones and trimethoprim-sulfamethoxazole.

All of the *S. lugdunensis* isolates in our study occurred as part of a mixed flora. Our policy has been to report CoNS only if pure growth occurs, and only those isolates are further tested for susceptibility to novobiocin to identify *S. saprophyticus* and for PYR hydrolysis and ornithine decarboxylation to identify *S. lugdunensis*. Among 43,941 urine cultures evaluated over a recent 12-month period in our laboratory, we have identified none with a pure growth of *S. lugdunensis*. Over the same time period, nine (0.02%) urine cultures yielded a pure growth of *S. saprophyticus*.

The clinical significance of *S. lugdunensis* isolated along with other (mixed) flora requires further study. As this organism can be part of the "normal" perineal flora (3, 6), it may contaminate urine during the collection process. Additional studies are required to determine whether larger versus smaller colony counts of *S. lugdunensis* in urine cultures are more clinically relevant. It is noteworthy, however, that Herchline and Ayers (3) found that *S. lugdunensis* was frequently isolated as part of a mixed flora. For 60% of all specimens (specimens were from multiple anatomic sites), *S. lugdunensis* was isolated as part of a mixed flora. It is believed that some of the patients in the present study were infected with the organism; for other patients, it was believed that the organism was a contaminant or represented colonization without infection. *S. lugdunensis* was the sole agent isolated from 40% of specimens from infected patients.

With the realization that significant morbidity can occur with extraurogenital *S. lugdunensis* infection and with the assumption that a source of extraurogenital infection may be the urinary tract, it may be as important if not more important to identify this CoNS pathogen than it is to identify *S. saprophyticus. S. saprophyticus* rarely causes extraurogenital disease and is less virulent than *S. lugdunensis*. The virulence of *S. lugdunensis* is thought to be due in part to the production of a δ-like toxin that shares homology with the δ-toxin of *S. aureus* (13). Nucleic acid sequences related to the *S. aureus* accessory gene regulator (*agr*), the major regulatory determinant of virulence, have also been demonstrated in *S. lugdunensis* (12).

In the present study the 30 patients from whose urine *S. lugdunensis* was isolated did not appear to have common underlying medical conditions that predisposed them to infection with this organism. A curious observation was that the majority (53%) of *S. lugdunensis* isolates occurred in women ages 65 years or older. The reason for this is unknown. Of interest, isolates of CoNS from women in this age range accounted for only 20% of the total isolates of CoNS recovered.

In summary, *S. lugdunensis* may be an unrecognized yet infrequent cause of UTI. Further prospective studies are required to determine the significance of this organism as a urinary pathogen. Additionally, studies are also required to

discern whether routine screening of urine cultures for *S. lugdunensis* is warranted.

We thank the technologists in the Bacteriology Laboratory for screening urine cultures for isolates of CoNS and Roberta Kondert for efforts in preparation of the manuscript.

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