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Frequency of Isolation of *Staphylococcus lugdunensis* among Staphylococcal Isolates Causing Endocarditis: a 20-Year Experience

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Eighty-nine staphylococcal isolates recovered from patients with bacterial endocarditis at the Mayo Clinic from 1980 to 1999 were studied to determine the prevalence of *Staphylococcus lugdunensis* among clinical isolates of staphylococci causing endocarditis. Four isolates, all from patients with native mitral valve endocarditis, were identified as *S. lugdunensis*.

Staphylococci cause 20 to 35% of cases of native valve infective endocarditis in non-intravenous drug users, and of these cases, the vast majority involve *Staphylococcus aureus* (8). Among the coagulase-negative staphylococci, *Staphylococcus epidermidis* is the most frequent infecting species and may cause both native valve endocarditis and, more commonly, prosthetic valve endocarditis (8). Native valve endocarditis due to *S. epidermidis* typically presents in an indolent fashion, whereas native valve endocarditis due to *Staphylococcus lugdunensis*, an organism first described in 1988, can be aggressive and is associated with high mortality (2, 3). The prevalence of *S. lugdunensis* among clinical isolates of staphylococci causing endocarditis is unknown. The purpose of this study was to determine the prevalence of *S. lugdunensis* among clinical isolates of staphylococci causing endocarditis.

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Beginning in 1970, Mayo Clinic endocarditis patients have been reported to the Mayo Clinic endocarditis registry, and for those cases where it has been convenient, the associated bacteria have been stored at −70°C. Eighty-nine staphylococcal isolates recovered from the blood of Mayo Clinic patients with endocarditis from 1980 to 1999 were studied. Staphylococcal isolates were subcultured onto blood agar plates; tube coagulase testing was performed using rabbit plasma, with readings taken at 4 h and overnight. Twenty-two isolates were tube coagulase negative. Latex agglutination testing to detect clumping factor and protein A (Staphaurex; Murex Biotech Limited, Kent, England) and pyrrolidonyl arylamidase testing (Remel, Lenexa, Kans.) were performed on the 22 tube coagulase-negative isolates. Twenty-one isolates were Staphaurex latex agglutination negative and one was Staphaurex latex agglutination positive. The Staphaurex-positive isolate and four of the Staphaurex-negative isolates were pyrrolidonyl arylamidase positive. Of these five pyrrolidonyl arylamidase-positive isolates, four were ornithine decarboxylase positive and were identified as *S. lugdunensis*. One of the four *S. lugdunensis* isolates was Staphaurex positive. All four *S. lugdunensis* endocarditis cases involved native valves, whereas only 5 of the other 18 (28%) tube coagulase-negative staphylococcal isolates involved native valves.

The medical records of the four patients with *S. lugdunensis* endocarditis were reviewed.

The first case was that of a 49-year-old man who underwent transplantation in 1983 with a kidney from a living relative. Nine weeks postransplant he developed fever and was found to have nine of nine blood culture bottles positive for a coagulase-negative staphylococcus (retrospectively identified as *S. lugdunensis*). Two-dimensional echocardiography demonstrated mitral valve prolapse with a probable ruptured chorda and mitral regurgitation. He was diagnosed with bacterial endocarditis and treated for 4 weeks with intravenous antibiotics (nafcillin and cefazolin). When seen in follow-up 12 years later, he was noted to have congestive heart failure secondary to mitral regurgitation.

The case of the second patient has been previously reported (2). He was a 39-year-old man who developed native mitral valve *S. lugdunensis* endocarditis after vasectomy (2). He was successfully treated with a 7-week course of intravenous antibiotics and subsequently underwent mitral valve reconstruction for severe mitral regurgitation (2).

The third case was that of an 85-year-old woman who developed *S. lugdunensis* left total-knee arthroplasty infection and mitral valve endocarditis in 1999. Transesophageal echocardiography revealed a 1.1- by 1.0-cm vegetation on the posterior leaflet of the mitral valve with probable perforation and a 0.9- by 0.7-cm vegetation on the anterior leaflet of the mitral valve with probable perforation and a ruptured chorda, with severe mitral regurgitation. She had undergone left total-knee arthroplasty 16 months earlier and had a history of mitral regurgitation. She underwent irrigation and debridement of her left knee (with retention of components) and was treated for 28 days with intravenous vancomycin followed by chronic oral minocycline suppression.

The fourth case was that of a 67-year-old man who developed *S. lugdunensis* mitral valve endocarditis in 1999. He had a history of mitral regurgitation related to rheumatic heart disease and cryptogenic cirrhosis. Transesophageal echocardiography revealed a 1.5- by 0.7-cm vegetation on the anterior leaflet of the mitral valve, with mild stenosis and moderate to severe regurgitation. He had lower-extremity and scrotal edema with concomitant scrotal skin breakdown. Blood cultures grew *S. lugdunensis*. He was treated with a 6-week course of antibiotics (vancomycin and ceftriaxone).

Our study is the first to define the prevalence of *S. lugdunen-*

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sis among clinical isolates of staphylococci causing endocarditis. We found that *S. lugdunensis* accounts for 18% of tube coagulase-negative staphylococci causing infective endocarditis and 44% of tube coagulase-negative staphylococci causing native valve endocarditis. Importantly, few microbiology laboratories have routinely identified *S. lugdunensis*. Depending on the methods used in the laboratory to identify staphylococci, *S. lugdunensis* may be identified as a coagulase-negative staphylococcus or may be misidentified as *S. aureus* (because some isolates produce clumping factor, resulting in positive slide coagulase or latex agglutination tests). Accurate identification of this organism when isolated from blood and other sterile sites may provide valuable clues to the physician as to its clinical significance. A previously published retrospective examination of 978 tube coagulase-negative staphylococcal blood isolates found no *S. lugdunensis* isolates (1). In our study, 44% of tube coagulase-negative staphylococci causing native valve endocarditis were *S. lugdunensis*. When *S. lugdunensis* is isolated from blood, a careful search for a source of infection should be performed and a diagnosis of infective endocarditis should be excluded (4). An association of *S. lugdunensis* endocarditis with inguinal skin breaks occurring in the context of vasectomy, femoral arterial catheterization, or inguinal furuncle has been previously reported (2, 6, 9). Those authors noted that the perineum is the normal habitat of *S. lugdunensis*. Of our four patients, one had undergone vasectomy (previously reported), one had a scrotal wound, and one had undergone renal transplantation; these cases are consistent with a perineal, pelvic, or inguinal cutaneous source of *S. lugdunensis*.

To date, 29 cases of infective endocarditis due to *S. lugdunensis* have been reported; these cases have recently been summarized by Fervenza et al. (2). Herein we report three new cases. Most *S. lugdunensis* endocarditis cases involve native, as opposed to prosthetic, valves (2). In the study by Frevenza et al., a poor response to conventional antimicrobial therapy, cardiac valvular destruction, myocardial abscess formation, and high mortality (58% of all cases reported in the literature) characterized *S. lugdunensis* endocarditis, despite susceptibility to oxacillin and often to penicillin (2).

An important question is whether oxacillin MIC breakpoints for coagulase-negative staphylococci or for *S. aureus* should be applied to *S. lugdunensis*. As an example, the oxacillin MIC for the fourth patient's *S. lugdunensis* isolate was 1 μg/ml; the organism was reported by the laboratory to be oxacillin resistant because it was a coagulase-negative staphylococcus (7). However, *S. lugdunensis* behaves the same way clinically as does *S. aureus* which would have been considered susceptible at this breakpoint; further, this isolate was beta-lactamase negative, the penicillin MIC for this isolate was 0.06 μg/ml, and it was *mecA* gene negative as determined by using a PCR assay (J. Uhl, P. Kohner, C. Kolbert, and F. Cockerill, Abstr. 100th Gen. Meet. Am. Soc. Microbiol., abstr. C-331, 2000.) The patient was treated with and cured using ceftriaxone, suggesting that the isolate could have been considered to be oxacillin susceptible. Antimicrobial susceptibility testing was performed on two of the third patient's *S. lugdunensis* isolates. The oxacillin MIC for an *S. lugdunensis* isolate from the knee was 1 μg/ml, and the oxacillin MIC for an *S. lugdunensis* isolate from the blood was >2 μg/ml. The organism was reported by the laboratory to be oxacillin resistant in both instances, and therefore the patient was treated with vancomycin; this organism was *mecA* gene negative as determined by using a PCR assay. The *S. lugdunensis* isolate from the first patient was also *mecA* gene negative using a PCR assay; the oxacillin MIC was 1 μg/ml. The second patient's isolate was unavailable for *mecA* gene testing; the oxacillin MIC was 1 μg/ml.

Of 18 isolates of *S. lugdunensis* examined in a recently published study, all were *mecA* gene negative, and the oxacillin MICs for all were ≥0.5 μg/ml (5). Therefore, the National Committee for Clinical Laboratory Standards recommendations for oxacillin MIC breakpoints for coagulase-negative staphylococci may not be appropriate for *S. lugdunensis* (7).

In conclusion, *S. lugdunensis* accounted retrospectively for 18% of tube coagulase-negative staphylococci causing infective endocarditis and 44% of tube coagulase-negative staphylococci causing native valve endocarditis. Species identification of *S. lugdunensis* isolates from sterile sites should be done routinely, as this may alter diagnostic and therapeutic approaches. Current National Committee for Clinical Laboratory Standards recommendations for oxacillin MIC breakpoints for coagulase-negative staphylococci may not be appropriate for *S. lugdunensis*.

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