Clinical Significance of Staphylococcus warneri Bacteremia

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Twenty-seven episodes of bacteremia caused by Staphylococcus warneri were identified at Long Island Jewish Medical Center in New York between 1984 and 1989. Fourteen of these were thought to represent true bacteremias and 13 to represent contaminants. Of the 14 true bacteremias, 5 were in pediatric and 9 were in adult patients. Eight of 14 patients (57%) had catheter-related bacteremia and 5 of 14 had bacteremia of unknown source. There was one case of fulminant native valve S. warneri endocarditis. All cases of catheter-related bacteremia, except one, were nosocomially acquired, and 75% of these patients had an underlying immunosuppressive condition. Only 40% of patients with bacteremias of unknown source were immunocompromised, and S. warneri appeared to be noninvasive in this group. Interestingly, all five of the pediatric isolates were oxacillin susceptible, although four of five were resistant to penicillin, despite the fact these patients were hospitalized an average of 29 days. In contrast, seven of nine adult isolates were resistant to both oxacillin and penicillin. The only case of native valve S. warneri endocarditis occurred in a patient who had no known underlying valvular heart disease, but had an underlying immunosuppressive condition. Identification to species level of coagulase-negative staphylococci may lead to appreciation of the importance of bacteria such as S. warneri as human pathogens.

Coagulase-negative staphylococci are now considered significant nosocomial pathogens complicating central venous catheters, prosthetic heart valves, prosthetic joints, and neurosurgical ventricular shunts and in infants in intensive care nurseries (1, 8, 12, 15, 20, 24–26, 28). Bacteremia with coagulase-negative staphylococci may be associated with significant morbidity and mortality in hospitalized patients. Such isolates can no longer be regarded only as contaminants (1, 21). Staphylococcus epidermidis is the most commonly isolated species of clinical importance (18, 19, 21, 23), while data on the clinical significance of other coagulase-negative staphylococci are limited, and few are available for Staphylococcus warneri (14).

This study evaluated the clinical significance and outcome of S. warneri bacteremia in both adult and pediatric patients, including a case of native valve endocarditis. This study documents the importance of S. warneri as a potential human pathogen and emphasizes the value of identifying coagulase-negative staphylococci to the species level, particularly when isolated from blood cultures in appreciable numbers.

MATERIALS AND METHODS

The medical records of all patients with S. warneri bacteremia between 1 January 1984 and 31 December 1989 at Long Island Jewish Medical Center were reviewed. Patients were identified by the records of positive blood cultures in the hospital’s division of microbiology. Both adult and pediatric patients were included. The following clinical information was obtained: age, sex, underlying disease, type of catheter if bacteremia was catheter related, number of positive blood cultures, antibiogram of the isolate, treatment, and outcome of infection.

Definitions. We classified patients into three broad categories.

(i) Catheter-related infections. The onset of bacteremia occurred within a few days of the placement of the catheter and/or the catheter tip yielded the same organism at the time of removal of the catheter. Catheter tips were cultured as described previously (10). These patients had one or more positive peripheral blood cultures.

(ii) Endocarditis. The patient with endocarditis had two or more positive blood cultures with clinical evidence of endocarditis.

(iii) Bacteremia of unknown source. These patients had two or more positive blood cultures with no definite source of S. warneri infection, no clinical evidence of endocarditis, and no other source of fever.

We considered S. warneri to be a contaminant if only one blood culture was positive, regardless of the number drawn, and there was no clear source for the bacteremia.

Patients were considered cured if signs and symptoms of infection were no longer present and the bacteremia was cleared.

Microbiology. Adult and pediatric isolator tubes (DuPont, Wilmington, Del.) were used to obtain all blood specimens for culture; they were processed in accordance with the manufacturer’s instructions. One 5% sheep blood agar plate (Becton-Dickinson Microbiology Systems [BBL], Cockeysville, Md.), two chocolate agar plates (BBL) and one Sabouraud agar plate (BBL) were each inoculated with approximately 0.3 ml of the sedimented (adult) and uncentrifuged (pediatric) specimen. The remaining 0.3 ml was added to 18 ml of a special broth, previously described (11), which permits the growth of all medically significant anaerobes. On isolation, S. warneri formed whitish, circular, slightly domed colonies, 2 to 3 mm in diameter on blood and chocolate agar within 24 h of incubation at 35°C. Several colonies from each primary isolation plate were transferred to blood and Staphylococcus 110 (BBL) agars and held for 72 h to ensure uniformity of colonial morphology. All isolates were coagu-
lase negative and were identified as *S. warneri* by the Staph-Ident systems (Analytab Products, Plainview, N.Y.) and the gram-positive identification card in the AutoMicrobic System (Vitek Systems, Hazelwood, Mo.). All isolates were identified independently as *S. warneri* by Wesley E. Kloos (North Carolina State University, Raleigh). None of the isolates produced acid from mannose but all produced acid from mannitol, two important reactions that distinguish *S. warneri* from *Staphylococcus lugdunensis* (14). Diffusion (3) and dilution (22) susceptibility studies were performed in strict compliance with published procedures.

RESULTS

Twenty-seven cases of *S. warneri* bacteremia were identified. According to the above definitions, 5 of 9 bacteremias in pediatric patients and 9 of 18 in adults represented true infections. The remainder were considered contaminants. For purposes of analysis, the 14 patients with true bacteremias were divided into pediatric and adult groups.

**Pediatric patients.** Table 1 summarizes the data on the five patients with *S. warneri* infections. The patients ranged in age from 26 weeks to 15 years, with a mean age of 39.6 months. Two of these patients were male, and three were female. Three of five patients were immunocompromised.

Four patients had catheter-related bacteremias, and one had bacteremia of unknown origin. Of the four patients with catheter-related bacteremia, two had Broviac catheters, one had an umbilical vessel, and one had a subclavian catheter. The catheters were in place from 8 to 15 days, with a mean of 12.2 days. Three of four patients had their catheters removed. One of these three patients received no antibiotics, while the other two received antibiotics for 10 and 21 days. The single patient who did not have his catheter removed received 2 weeks of appropriate antibiotics and was cured. The patient with bacteremia of an unknown source received 7 days of inappropriate antibiotics and recovered.

The isolates from four of the five patients were resistant to penicillin but susceptible to oxacillin. The fifth isolate was susceptible to both penicillin and oxacillin. All isolates were susceptible to vancomycin.

All five patients cleared their bacteremia and were considered cured, including the patient with bacteremia of unknown source who received inappropriate antibiotics.

**Adult patients.** Table 2 summarizes the data on the nine adult patients with *S. warneri* bacteremia. The patients ranged in age from 33 to 77 years, with a mean age of 60.5 years, and included six patients who were immunocompromised. Six of these patients were male, and three female.

Four patients had catheter-related bacteremia. The patient with native valve endocarditis was a 64-year-old male with no history of congenital heart disease or rheumatic fever who was admitted with fever, subconjunctival hemorrhages, splinter hemorrhages, multiple petechiae, splenomegaly, and a systolic murmur. Four of six blood cultures were positive for *S. warneri*. Despite treatment with vancomycin and gentamicin, the patient developed a new diastolic murmur of aortic insufficiency and deteriorated neurologically. He died after 15 days of hospitalization. Autopsy revealed friable vegetation on the mitral, aortic and pulmonary valves consistent with endocarditis. Splenic infarcts and septic emboli to the kidneys were also noted. Of the four patients with bacteremias of unknown origin, two had localized abscesses which grew other organisms; these lesions were not considered the source of the *S. warneri* bacteremia.

Of the four patients with catheter-related bacteremia, two patients had central venous pressure lines, one had a triple lumen, and one had a Swan-Ganz catheter. The catheters were in place from 3 to 14 days (mean, 8 days) and were removed in three patients at the time of onset of bacteremias. Patients received antibiotics for a duration of 5 to 15 days, with a mean of 6.7 days. All patients with catheter-related infections cleared their bacteremia and were considered cured. One patient who received no antibiotics and did not have his catheter removed also recovered.

Three of the four patients with bacteremia of unknown origin received antibiotics for 2 to 7 days, with a mean of 4 days. These three patients responded to therapy. One patient received inappropriate antibiotics and remained febrile 2 weeks after his blood cultures were positive. One patient died of causes unrelated to *S. warneri* bacteremia.

Five of the nine isolates were resistant to oxacillin and penicillin. Three were resistant to penicillin but susceptible to oxacillin, and one was susceptible to both penicillin and oxacillin. All nine isolates were susceptible to vancomycin.

**DISCUSSION**

Coagulase-negative staphylococci have emerged in recent years as important nosocomial pathogens, with *S. epidermidis* the most frequently recognized organism in this group (27). *S. warneri* and other coagulase-negative staphylococci have been recognized less frequently as significant human pathogens (17). Additionally, *S. warneri* represents only 1% of the skin staphylococci in normal individuals (6). *S. warneri* is distinguished from *S. epidermidis* by its lack of phosphatase and its ability to produce acid from trehalose (14).

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Underlying disease</th>
<th>Type of catheter</th>
<th>No. of days catheter in place</th>
<th>No. of positive blood cultures/ no. drawn</th>
<th>Antibiotic susceptibility</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catheter-related</td>
<td>1</td>
<td>27 mo</td>
<td>F</td>
<td>Renal failure</td>
<td>Subclavian</td>
<td>8</td>
<td>2/2</td>
<td>Pen' Ox*</td>
<td>Catheter removed; no antibiotic</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>15 yr</td>
<td>M</td>
<td>Short bowel syndrome</td>
<td>Broviac</td>
<td>14</td>
<td>1/1</td>
<td>Pen' Ox*</td>
<td>Catheter not removed; 14 days of appropriate antibiotic</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>36 wk</td>
<td>F</td>
<td>Gastrochisis</td>
<td>Broviac</td>
<td>12</td>
<td>2/2</td>
<td>Pen' Ox*</td>
<td>Catheter removed; 3 wk of appropriate antibiotic</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>26 wk</td>
<td>M</td>
<td>Prematurity</td>
<td>UV line</td>
<td>15</td>
<td>1/1</td>
<td>Pen' Ox*</td>
<td>Catheter removed; 10 days of appropriate antibiotic</td>
</tr>
<tr>
<td>Unknown source</td>
<td>5</td>
<td>8 days</td>
<td>F</td>
<td>C-section</td>
<td>None</td>
<td>2/2</td>
<td>Pen' Ox*</td>
<td>7 days of inappropriate antibiotic</td>
<td>Cured</td>
</tr>
</tbody>
</table>

* Pen, penicillin; Ox, oxacillin.
In the 5-year period between 1984 and 1989, we identified 27 episodes of *S. warneri* bacteremia among adult and pediatric populations, 14 (51.8%) of which were considered clinically significant. *S. warneri*, like *S. epidermidis*, was most frequently associated with intravascular catheter infections, representing 57% of infections in this study. Seventy-five percent of patients with catheter-related bacteremia had underlying immunosuppressive illnesses. Catheters were in place for an average of 10.1 days prior to the episode of bacteremia. All cases of catheter-related bacteremia were nosocomially acquired, except for patient 1, who had a positive blood culture after 1 day of hospitalization, although he had a Broviac catheter in place for a year.

The *S. warneri* isolates from the pediatric patients differed from those recovered from adults by their susceptibility to oxacillin. In the pediatric patients, all isolates were susceptible to oxacillin and one of four was susceptible to penicillin as well, whereas three of four adult isolates were resistant to both oxacillin and penicillin. Usually, antibiotic resistance patterns suggest the nosocomial origin of coagulase-negative staphyloccoci (5, 13), particularly in patients with indwelling intravascular catheters. It is somewhat surprising, therefore, that the *S. warneri* isolates from hospitalized pediatric patients with catheter-related infections were susceptible to oxacillin. Six of eight patients had their catheters removed and received antibiotics for an average of 8.9 days. Of the remaining two patients in whom the catheters were left in place, one received antibiotics while the other did not. All patients with catheter-related bacteremia were apparently cured.

It is interesting to note that the adult case of native valve endocarditis occurred in a patient with no known underlying congenital or rheumatic heart disease. Most cases of native valve endocarditis caused by coagulase-negative staphylococci have an underlying valvular defect (2, 4, 6, 9, 16), while only one such case has been reported as due to *S. warneri* (6). This patient's underlying cirrhosis may have predisposed him to serious infection with *S. warneri*, in view of the increasing recognition of coagulase-negative staphylococci as pathogens of immunocompromised patients (2, 8).

Two of five patients with bacteremia of unknown origin were immunocompromised. All blood cultures were drawn when patients manifested signs and symptoms of infection, e.g., elevated white blood cell count and a toxic appearance. Since this was a retrospective study, it is difficult to be certain that positive blood cultures in a given individual were, in fact, drawn at separate times. However, the general practice at this hospital is to draw two blood cultures at separate times. With the exception of patient 11, who had acute myelocytic leukemia and died secondary to respiratory failure, all patients were cured of their infection whether or not the antibiotics utilized were considered appropriate. Although these patients appeared to have true bacteremias, *S. warneri* may cause less serious disease in immunocompetent individuals than in those who are immunocompromised.

This study suggests that *S. warneri* may be a nosocomial pathogen, especially in catheter-related infections. In immunocompromised patients, *S. warneri* may cause serious invasive infections, including endocarditis on native heart valves. Although some studies have suggested that identification of coagulase-negative staphylococci may have limited...
utility (7, 23), this study emphasizes the importance of such analyses in coagulase-negative staphylococcal bacteremias.

REFERENCES

Letters to the Editor

CLEARVIEW Chlamydia Test for Detection of Chlamydiae in Cervical Specimens

In their evaluation of the CLEARVIEW Chlamydia test, a rapid immunoassay for the direct detection of *Chlamydia trachomatis* from cervical specimens, Stratton et al. (1) reported that 14 of 677 (2%) cervical specimens failed to migrate in the CLEARVIEW test. We conducted a study between February and May 1991 in which 23 private gynecologists volunteered to participate. Each woman visiting their clinics during that period was asked to participate, and if consent was given a cervical specimen was then systematically taken, unless cervical bleeding was too heavy. A questionnaire was filled out by every patient included in the study. We used the CLEARVIEW test to analyze the cervical specimens.

Nine hundred and thirty cervical specimens were analyzed; 22 (2.4%) were positive and 17 (1.8%) failed to migrate in the CLEARVIEW test and were considered uninterpretable. We compared characteristics of these 17 women to those of either positive or negative women. There was no difference in the permeabilities of the cervixes. No lubricant was used with the vaginal speculum by the physicians who took the uninterpretable specimens, except, rarely, some water. The mean delays between sampling and laboratory testing did not differ between uninterpretable specimens and negative or positive ones. In 58% of the uninterpretable specimens (versus 9.5% of the positive and 12.8% of the negative specimens), swab-induced bleeding was reported, and in 31.3% (versus 4.8% of the positive and 9% of the negative), spontaneous bleeding (menstrual or metrorrhagia) was noted. This suggests that the presence of blood on the swab may prevent the migration of the extracted specimen in the CLEARVIEW test. However, no bleeding was reported in 35% of the uninterpretable specimens. A possibility which could be investigated is the presence of cervical mucus on the swab. Further research is needed to establish all the reasons for the failure to migrate in the CLEARVIEW test and the best conditions of use for this test.

REFERENCE


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Ed. Note: The authors felt that no response was necessary.

Significant Infection Caused by *Staphylococcus warneri*

Kamath et al. recently reported 27 episodes of bacteremia caused by *Staphylococcus warneri* identified in their institution between 1984 and 1989 (5). Among the nine true bacteremias in adult patients, there was one case of community-acquired native valve endocarditis in a 64-year-old man without known valvular heart disease. The patient died after 2 weeks of medical therapy, and autopsy revealed mitral, aortic, and pulmonary valve vegetations as well as splenic infarcts and septic renal emboli. Cirrhosis was cited as a possible predisposing disease. One previously reported case of native valve endocarditis caused by *S. warneri* following vasectomy in a 32-year-old man without known valvular heart disease was cited (3). This patient required aortic valve replacement in addition to medical therapy for cure. Small vegetations and ulcerative destruction of the noncoronary cusp of the aortic valve were found at surgery. No predisposing cause for infection was identified. On the basis of these two cases, the authors concluded that *S. warneri* may cause serious, invasive infection.

Considerable additional data support the pathogenic role of *S. warneri*. Five additional cases of native valve endocarditis have been reported: one was a well-characterized case report (8) and four were from two series which reported cases of native valve endocarditis caused by coagulase-negative *staphylococci* (2, 4). I reported a community-acquired episode which occurred in a 66-year-old man without valvular heart disease (8). He required both aortic and mitral valve replacements. Extensive destruction of both valves and an aortic valve ring abscess were found at surgery. No significant predisposing cause was evident. Caputo et al. reported three cases in which *S. warneri* was isolated from patients meeting strict criteria for native valve endocarditis (2). All of these isolates were community-acquired. Etienne and Eykyn reported one case caused by *S. warneri* in their series of 35 patients with native valve endocarditis caused by coagulase-negative *staphylococci* (4). *S. warneri* has also been reported to have caused three cases of hematogenous vertebral osteomyelitis (1, 6, 8). One of these infections was attributed to an infected Hickman catheter (1), whereas the others were caused by community-acquired bacteremias. In addition, occult infection with *S. warneri* has recently been implicated as the etiological agent in three cases of femoral anaesthetic pseudoaneurysms associated with prosthetic vascular grafts (7).
It is clear that *S. warneri* has the potential to cause significant community-acquired and nosocomial infections. In particular, native valve endocarditis may present as acute, aggressive disease, requiring a combined medical and surgical approach because of valve destruction or abscess formation. Routinely identifying clinically significant isolates of coagulase-negative staphylococci to the species level will clarify the frequency and spectrum of disease caused by these increasingly important pathogens.

REFERENCES


**Author’s Reply**

We appreciate Dr. Wood’s comments regarding our article. Dr. Wood correctly refers to a case of native valve endocarditis due to *S. warneri* that he reported (3). As in our study, his patient had no evidence of prior valvular heart disease. Caputo et al. described 21 patients with native valve endocarditis caused by coagulase-negative staphylococci (1). Of the 16 isolates studied, 3 were *S. warneri*. However, 14 of the 21 patients had preexisting valvar or congenital heart disease. It is not clear whether the three cases of *S. warneri* endocarditis occurred in patients without preexisting valvar heart disease. Similarly, Etienne and Eykyn reported 35 cases of native valve endocarditis due to coagulase-negative staphylococci, of which 1 was due to *S. warneri* (2). Seventy-four percent of these patients had some underlying cardiac abnormality. The authors do not comment on whether the patient with *S. warneri* endocarditis had preexisting valvar or congenital heart disease.

Again, we regret not including Dr. Wood’s case report. His comments serve to further emphasize the potential importance of *S. warneri* as a human pathogen.

REFERENCES


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