

Staphylococcus simulans Septicemia in a Patient with Chronic Osteomyelitis and Pyarthrosis

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***Staphylococcus simulans* was identified as the etiological agent of osteomyelitis and septic arthritis in an adult male who had sustained a fracture of the fibula and syndesmosis separation which required the installation of orthopedic hardware. Identifying characteristics and antibiograms for this organism, recovered from blood, wound exudate, and deep tissue samples, were determined. Recent evidence has linked slime production (adherence to smooth surfaces) by coagulase-negative staphylococci to infections by these organisms at sites where foreign bodies had been inserted. Tests for adherence showed this *S. simulans* strain to be a strong slime producer. This is the first reported case of osteomyelitis and septicemia due to *S. simulans*.**

Staphylococcus simulans is a coagulase-negative staphylococcus (C-NS) occasionally found on human skin (13) and in the urethras of healthy women (19). Its clinical significance has not been established, since it is rarely identified in association with infections. On infrequent occasions it has been isolated from clinical specimens, such as blood, urine, fluids, and exudates from wounds, abscesses, and lesions (10, 20), as well as from intravascular catheters (9). Most isolates are susceptible to antimicrobial agents, i.e., the aminoglycosides, penicillins, sulfonamides, erythromycin, cephalothin, cefoxitin, chloramphenicol, clindamycin, tetracycline, and vancomycin (10, 20).

This report concerns a patient who underwent open reduction of a fibular fracture and subsequently developed osteomyelitis and pyarthrosis with sepsis from *S. simulans*. The organism was recovered from blood, wound exudate, and all deep tissue specimens from the infected ankle.

Case report. A 39-year-old male fell from a tree in November 1982 and sustained a closed fracture of the lower right fibula and syndesmosis separation. An open reduction with internal fixation by insertion of fibular plating and a syndesmosis screw was performed at a local community hospital. The patient subsequently developed an infection leading to anterior compartment syndrome, with loss of sensation down to the great toe. Fasciotomies, followed by multiple surgical debridements and medial and lateral longitudinal skin grafts, were performed over the following 3 months. Laboratory findings from this period of hospitalization were unavailable.

In February 1983 the patient was hospitalized for several days at Erie County Medical Center for removal of the syndesmosis screw. Examination at that time showed drainage from the area of the medial malleolus with some scabbing. There were no other clinical findings.

No written record of the patient's progress was available until he was readmitted to Erie County Medical Center in November 1983, complaining of pain, a throbbing sensation in the right ankle, nausea, shaking chills, and diaphoresis. On admission he appeared septic with a temperature of 40°C. Examination revealed redness and swelling of the right ankle, with drainage from the medial malleolus area. A

purulent discharge from areas of the right great toe and ankle had been noted throughout a 3-month period before this readmission. X-rays of the joint region showed significant changes compared with those taken 4 months previously, which were consistent with the diagnosis of septic arthritis secondary to chronic osteomyelitis. Laboratory findings showed an elevated peripheral leukocyte count of 11,900 per mm³ with a normal differential and platelet count. Ankle drainage specimens and two blood culture sets were taken at this time. A Gram stain of the wound exudate showed gram-positive cocci. The patient was given empirical therapy of tobramycin and oxacillin.

On day 2 of hospitalization, surgical debridement of the infected ankle and arthrotomy were performed, with installation of a Penrose drain. Wound exudate and pockets of purulent material external to and within the capsular space (deep tissue specimens) were cultured for aerobic and anaerobic organisms. Examination of Gram-stained films of all specimens revealed gram-positive cocci in only the wound exudate. Catalase-positive, gram-positive cocci, later identified as *S. simulans*, were isolated from all ankle specimens and from both blood culture sets by day 3.

Tobramycin therapy was discontinued at this time. Oxacillin therapy was replaced by penicillin G on day 4 on the basis of antibiograms of wound and blood isolates and subsequent determination of MICs and MBCs for each antimicrobial agent. The patient responded to therapy and was afebrile by day 6. Drainage from the sinus tract persisted but was diminished. The Penrose drain was removed on day 9 of hospitalization. On days 5 to 11, peripheral leukocyte counts and differentials were normal but were accompanied by persistently elevated erythrocyte sedimentation rates of 48, 56, and 40 mm/h. Platelet counts were elevated at 530,000 and 473,000 per mm³ on days 9 and 11, respectively. Pathological and operative findings confirmed the clinical diagnosis of osteomyelitis with septic arthritis. Because of persistent intravenous catheter infiltration, the patient was switched to oral medications by day 9 and was discharged 16 days after admission.

Microbiology. Pure cultures of C-NS strains were isolated from blood samples, the draining sinus, and two deep tissue sites in the infected right ankle. Anaerobic bottles (Bactec 7D medium; Johnston Laboratories, Becton Dickinson & Co., Towson, Md.) from two blood culture sets were posi-

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TABLE 1. Characteristics of *S. simulans* isolates

Test	Results ^a
Colony morphology (5 days)	3 mm, yellow tint
Anaerobic growth in thioglycolate	Dense, uniform
Lysostaphin (200 µg/ml)	Susceptible
Bacitracin (Taxo A disk)	Resistant
Acid aerobically from glycerol-erythromycin (0.4 µg/ml) medium	No growth
Acid anaerobically from glucose	+
Hemolysis (human blood)	Moderate (2mm)
Coagulase	-
Urease	+
Nitrate reduction	+
Alkaline phosphatase	±
L-Arginine utilization	±
Acid aerobically from:	
Glycerol	+
β-D(-)-Fructose	+
α-Lactose	±
Maltose	-
D-Mannitol	+
D(-)-Ribose	±
Sucrose	+
D(+)-Trehalose	+
D(+)-Xylose-L(+)-arabinose	-
Xylitol	-
Novobiocin (5-µg disk)	Susceptible
Slime production	Strong

^a Symbols: +, positive result; -, negative result; ±, weak positive result.

tive by radiometric detection after 2 days of shaker incubation. Aerobic cultures of the same organism were isolated from all wound sites on blood-based medium; anaerobic cultures were negative for other organisms.

Five different criteria were used to characterize the isolates as staphylococci or micrococci (Table 1). On the basis of their resistance to bacitracin (7), anaerobic growth in thioglycolate medium (14), susceptibility to lysostaphin (15), and the production of acid anaerobically from glucose (22), all isolates proved to be *Staphylococcus*. Use of glycerol-erythromycin (0.4 µg/ml) medium (21) proved unsatisfactory, since all isolates failed to grow in the presence of this erythromycin concentration. The concentration of erythromycin used exceeded the corresponding MIC for these isolates (see below). Each isolate grew and produced acid aerobically from glycerol without erythromycin.

Species identity was determined by conventional methods (Table 1), by using the scheme described by Kloos and Schleifer (14). The tests used have been described previously (14). Detection of alkaline phosphatase activity was done by the plate method (2), and detection of arginine utilization was done with Moeller decarboxylase medium (16). Controls included a clinical isolate of *Micrococcus* and *S. aureus* ATCC 25923. Isolates exhibited identical colony morphology, growth patterns, and biochemical characteristics and were identified as *S. simulans*.

The species identity was also determined with the use of the API Staph-Ident System (Analytab Products, Inc., Plainview, N.Y.). The patterns of reactions by this system were identical for each isolate: β-glucosidase, mannose, mannitol, and salicin were negative (mannitol was positive by the conventional method); urease, trehalose, and β-galactosidase were positive; and alkaline phosphatase, β-glucuronidase, and arginine were weakly positive and difficult to interpret after the recommended 5-h incubation period. On the basis

of the suggestion of Doern et al., the test strip was reincubated for an additional 19 h (6). These three tests were confirmed as positive. The final profile number was 3461, an "excellent identification" of *S. simulans*.

Recent evidence suggests that slime production of C-NS isolates contributes to the establishment of infection by these organisms in the presence of a foreign body (1, 3, 4). Strong slime production (adherence to smooth surfaces) by the *S. simulans* isolates was detected by noting the adherence of bacterial growth in broth to test tube walls (3). Results were compared with those of known slime producers and nonproducers.

One isolate each from blood and deep tissue samples was examined and found to be susceptible to all antimicrobial agents tested by the disk diffusion method. The corresponding MICs (in micrograms per milliliter) were determined for the blood isolates and were found to be as follows: ampicillin, ≤0.25; cefamandole, ≤0.5; cefoxitin, ≤1; cephalothin, ≤0.25; chloramphenicol, 8; clindamycin, ≤0.12; erythromycin, 0.25; oxacillin, ≤0.12; penicillin, ≤0.03; tetracycline, 1; and vancomycin, ≤0.5. MBCs were equivalent.

Discussion. This is the first documented case of osteomyelitis with sepsis caused by *S. simulans*. The incidence of C-NS isolates is rare. Until recently, C-NS isolates were not characterized to the species level, and staphylococci not identified as *S. aureus* were labeled *S. epidermidis*. In a recent report, C-NS species, *S. epidermidis*, *S. haemolyticus*, and *S. capitis*, were associated with bone and joint infections (20). Indeed, most C-NS infections are caused by relatively few species, i.e., *S. epidermidis*, *S. haemolyticus*, *S. hominis*, and *S. warneri* (10, 20). These same organisms are the more prevalent C-NS strains found on human skin (13). The question of whether the number of infections may be attributable to a greater degree of virulence or enhanced opportunity of these species to cause infection has been raised (20). The rarity of *S. simulans* associated with infections may simply reflect the infrequent occurrence of this species on the skin, the inability to correctly identify this organism, or both.

Osteomyelitis due to C-NS isolates has been documented (20, 23) and is frequently a postsurgical complication following insertion of orthopedic appliances for reduction of fractures (23) and in total hip arthroplasty (8). Bacteremia is a common finding in bone and joint infections (5, 12). The association of C-NS infections with colonization of prosthetic devices is well known (18). This has been demonstrated, not only for bone and wound infections after insertion of orthopedic appliances, but in cases of intravascular catheter sepsis (24), prosthetic valve endocarditis (11), infections of cerebrospinal fluid shunts (1), and infected vascular prosthetic grafts (17). These infections are believed to arise by direct extension of skin flora into wound and catheter entry sites. Removal of the device is frequently required to eliminate infection (11, 17, 24). Slime production has been linked to the ability of C-NS isolates to colonize cerebrospinal fluid shunts (1) and intravascular catheters, resulting in sepsis (3). Additional evidence of the importance of slime production in infections associated with foreign bodies has come from experimental infections in mice: infections occurred only in the presence of implanted catheter tubing and were significantly increased in number for a slime-producing C-NS strain compared with a nonproducer (4).

The *S. simulans* strain isolated from this patient was a strong slime producer. This property could have contributed to the establishment of infection after introduction of the

organism into the surgical wound by contamination from adjacent areas of the skin of the patient.

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