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Catheter-Related Bacteremia Associated with Coagulase-Positive *Staphylococcus intermedius*

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We report a case of catheter-related bacteremia in a 63-year-old patient caused by *Staphylococcus intermedius*. Clinical resolution of the infection was obtained after removal of the intravenous device and antibiotic treatment. This observation emphasizes the risk of confusion between *S. intermedius* and *Staphylococcus aureus* if only a coagulase test is done.

Staphylococcus intermedius was first described in 1976 (5) and is the predominant coagulase-positive staphylococcus in the mouth and in skin infections of dogs. It has been cultured from the gingiva of 53 of 135 (39%) healthy canines (11) and has also been found in a wide range of other animal species including pigeons, dogs, minks, cats, foxes, raccoons, gray squirrels, goats, and horses (1, 3, 5).

In human beings, *S. intermedius* has rarely been found, even among individuals with frequent exposures to animals. In an investigation of the nasopharyngeal flora of healthy veterinary staff, *S. intermedius* was found in only 1 of the 144 persons investigated (12). It is, however, a common and potentially invasive zoonotic pathogen of canine-inflicted human wounds (7, 11) and has also been isolated as a pure growth in cultures of specimens from three individuals with non-canine-inflicted wounds (7): two clinically infected varicose leg ulcers in elderly patients and one infected suture line in a 13-year-old patient. Two of these patients were dog owners, and the other patient had contact with a dog 8 weeks before the isolation. One case of infective endocarditis has been described in a 17-year-old human immunodeficiency virus-positive patient with tricuspid insufficiency and echographic evidence of a vegetation on the anterior tricuspid valve (8). No obvious portal of entry was detected, but the right-sided infective endocarditis suggested contamination of the material for intravenous drug injection. *S. intermedius* was also considered to be the etiologic agent in an outbreak of food intoxication involving butter-blend products and resulting in more than 265 cases of infection in the western United States; all of the isolates were reported to produce enterotoxin A, unlike all of the control isolates (6). In fact, the true frequency of *S. intermedius* in non-canine-inflicted wounds remains unclear, because it can be confused with *Staphylococcus aureus* in medical laboratory analysis on the basis of coagulase production.

In this report, we described a patient with lung cancer who developed catheter-related bacteremia caused by *S. intermedius.*

In November 1983, a non-small cell lung carcinoma with splenic metastasis was diagnosed in a 63-year-old patient, and in December 1993, a permanent intravenous device (Portocath) was implanted for chemotherapy. In May 1994, he underwent a splenectomy, and because of a pulmonary recurrence of the tumor, chemotherapy was complemented with thoracic radiotherapy. In September 1994, a cerebral metastasis was diagnosed, and in October 1994 a pulmonary embolism caused by tumor recurrence occurred. He returned home on November 15 with no intravenous drug prescription, but because he was very weak, his general practitioner suggested vitamin supplements intravenously, and a daily injection was given through the intravenous device by a home nurse. To facilitate injection, the nurse left a ramp (one-way stop cock) permanently connected to the device by a curved needle. On November 20, the patient became febrile (38.5°C). He was admitted to the hospital 10 days later for chemotherapy and had a fever of 39°C. The curved needle was still inserted through the intravenous device, and there was a peripheral inflammation of the skin contiguous to the device. His leukocyte count was 12.1×10^9/liter, with 85% polymorphonuclear leukocytes and an erythrocyte sedimentation rate of 50 mm/h. Three sets of blood samples for culture were withdrawn through the intravenous device over a period of 12 h, and the patient was treated intravenously with amoxicillin-clavulanic acid (1 g every 8 h) and ciprofloxacin (200 mg every 12 h). The intravenous device was removed just after the beginning of the antibiotic treatment, and the catheter tip was cultured. All six bottles of the blood cultures and the catheter tip yielded a pure growth of gram-positive cocci which were catalase positive. The coagulase tube test was performed with citrated rabbit plasma coagulase (bioMérieux, Marcy-L'Etoile, France) or in the presence of EDTA (Difco Laboratories, Detroit, Mich.). Fibrinogen affinity factor (clumping factor) was evaluated by the Staphyslide agglutination test (bioMérieux), and heat-stable DNase was evaluated with a diagnostic kit (Sanofi Diagnostics Pasteur, Marnes-la-Coquette, France). Biochemical identification with the ID32 Staph gallery (bioMérieux) resulted in identification of the organism as *S. intermedius*. The phenotypic characteristics of the four isolates of *S. intermedius* are listed in Table 1 and were compared with those of the reference strains *S. intermedius* CCM5739 (5) and *S. aureus* CCM885.

All *S. intermedius* isolates were susceptible to most antistaphylococcal antibiotics (Table 2), and the patient's antibiotic treatment was not changed because he was apyretic. Antibiotic treatment was continued for a total of 10 days. On

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TABLE 1. Biochemical characteristics of the strains

Characteristic	*S. intermedius* (patient's isolates)	*S. intermedius* CCM5739	*S. aureus* CCM885
Tube coagulase	+	+	+
Heat-stable DNase	−	+	+
Clumping factor	−	−	+
Resistance to:			
Novobiocin	S[a]	S	S
Nitrofurantoin	S	S	S
Nitrate reduction	+	+	+
Urease	+	+	+
Arginine dihydrolase	+	−	+
Ornithine decarboxylase	−	−	−
Alkaline phosphatase	+	+	+
Acetoin production	−	−	+
β-Galactosidase	+	+	−
Acid production from:			
Glucose	+	+	+
Mannose	+	+	+
Maltose	+	+	+
Lactose	+	+	+
Trehalose	+	+	+
Mannitol	−	+	+
Raffinose	−	−	−
Sucrose	+	+	+
Turanose	−	+	+
Arabinose	−	−	−
Ribose	+	+	−
Cellobiose	−	−	−

[a] S, susceptible.

December 9, the patient was discharged from the hospital with clinical resolution of the infection.

Since the patient owned a cat and because *S. intermedius* has been isolated from household cats (3), swab samples from the nose, throat, gingiva, and rectum of the cat were obtained, but no *S. intermedius* strains were isolated. The home nurse was the owner of two dogs, but samples from his nose yielded no *S. intermedius*, only *S. aureus.*

In routine medical laboratory practice, the production of coagulase is frequently used as the criterion to distinguish *S. aureus* from other staphylococci, since other coagulase-positive staphylococcal species such as *S. hyicus*, *S. schleiferi* subsp. *coagulans*, or *S. intermedius* have been found only occasionally in human beings. In practice, the use of the coagulase tube test to identify *S. aureus* may lead to a number of misidentifications (i) because of the absence of coagulase production by true *S. aureus* isolates (4% of *S. aureus* isolates sent to the French National Reference Center for Staphylococci [13]), (ii) because of the production of proteases (pseudocoagulases) capable of digesting prothrombin and/or plasminogen and thereby promoting clotting in the absence of staphylocoagulase (this has been described for *S. schleiferi* subsp. *schleiferi* [15]); (iii) in cases of zoonotic infection caused by *S. intermedius*: Talan et al. (11) reanalyzed 14 strains of coagulase-positive staphylococci from infected wounds caused by dog bites and found that three of the isolates were *S. intermedius*. Other characteristics of *S. aureus*, such as the presence of a bound protein A, a fibrinogen affinity factor (clumping factor), and a heat-stable DNase, are useful for completing the identification of *S. aureus*, but *S. intermedius* also produces a heat-stable DNase which displays a significant degree of homology with that of *S. aureus* (2). A clear separation of *S. intermedius* from *S. aureus* is apparent only on the ID32 Staph strip when analyzing the API database; β-galactosidase activity and ribose acidification separate the isolates (99% of the *S. intermedius* isolates versus 1% of the *S. aureus* isolates for these two characteristics). Talan et al. (11) found that both species could also be differentiated by the acetoin reaction (0% of the *S. intermedius* isolates versus 100% of the *S. aureus* isolates), but 18% of *S. intermedius* strains were positive in the API database.

TABLE 2. In vitro antimicrobial susceptibility of *S. intermedius* isolated from blood

Antimicrobial agent	MIC (μg/ml)
Penicillin G	≤0.03
Oxacillin	≤0.03
Kanamycin	≤0.125
Gentamicin	≤0.125
Chloramphenicol	2
Doxycycline	4
Erythromycin	0.25
Lincomycin	0.25
Pristinamycin	0.125
Rifampin	≤0.25
Co-trimoxazole	≤0.03/0.57
Pefloxacin	≤0.25
Fosfomycin	≤1
Vancomycin	0.5
Teicoplanin	≤0.5

The staphylocoagulase produced by *S. intermedius* resembles that of *S. aureus* in its rate and method of action on prothrombin, but it is produced in lesser amounts (9). We detected no DNA homology by Southern blot hybridization between our four *S. intermedius* isolates or the reference strain with the *S. aureus* coagulase gene, using a specific probe as described previously (14).

The *S. intermedius* isolates from our patient were susceptible to most antistaphylococcal antibiotics except doxycycline (Table 2). Talan et al. (11) found that 72% of *S. intermedius* isolates were resistant to penicillin G but not to oxacillin. Resistance to chloramphenicol, macrolide-lincosamide antibiotics, and tetracycline mediated by various plasmids has been described in isolates from dogs (4). Tetracycline resistance has been characterized in *S. intermedius* strains from animals (10).

Identification of *S. aureus* on the basis of coagulase detection alone leads to a number of misidentifications which could be avoided by the use of a second test such as fibrinogen affinity factor detection. Any discrepancy between the two tests must be resolved by determining the biochemical characteristics of the isolates with a commercial gallery, which ensured the diagnosis of *S. intermedius* infection in the case reported here. An improvement in the species identification of staphylococci isolated in clinical laboratories should enable a better assessment of their true clinical significance, epidemiology, and pathogenic potential.

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