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***Leuconostoc* Species as a Cause of Bacteremia: Two Case Reports and a Literature Review**

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Two new cases of significant bacteremia caused by *Leuconostoc* spp. are reported and five others described in the literature are reviewed. Four of the seven patients were under one year old and presented with prolonged diarrhea related to gastrointestinal disorders. The remaining three patients were over 50 years of age and being treated in intensive care units. Six patients had nosocomially acquired catheter-related bacteremia. *Leuconostoc* spp. are naturally resistant to vancomycin, and five patients had received this antibiotic for prior bacteremia caused by methicillin-resistant staphylococci. The majority of patients presented with fever without severe complications. Penicillin is the treatment of choice and there is no report of any death directly attributable to infection by these microorganisms. Infection with *Leuconostoc* spp. should be suspected if "vancomycin-resistant streptococci" are isolated from the blood, and recorded as a potential cause of bacteremia in patients with indwelling intravenous catheters.

Leuconostoc spp. are gram-positive coccobacilli which belong to the lactic acid bacteria group (1). They are used in industrial microbiology in the production of wine, dairy products and dextrans (2). They are naturally resistant to vancomycin since the cell wall fails to provide a target for this antibiotic (1). Although they have occasionally been isolated from vaginal and stool samples (3), *Leuconostoc* spp. are not a regular part of the normal human flora.

Leuconostoc spp. are not generally considered to be a human pathogen (4), but sporadic cases of pneumonia (5, 6), meningitis (7), infection of peritoneal dialysis fluid (8), and bacteremia (5, 6,

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9–12) caused by this microorganism have recently been reported. We report two new cases of *Leuconostoc* bacteremia, and review five others described in the literature.

Case Reports. Case no. 1. A 2-month-old girl was admitted to hospital in February 1988 with refractory diarrhea, fever and failure to thrive. She received prolonged parenteral nutrition by different central catheters and several courses of broad-spectrum antibiotics, until a diagnosis of primary intolerance to monosaccharides was reached at seven months of age. Her clinical course was further complicated by two episodes of catheter-associated *Staphylococcus epidermidis* bacteremia, treated with i.v. vancomycin on both occasions. Fifteen days after the last course of vancomycin, the patient presented with a new episode of fever. Three blood cultures were obtained and vancomycin was recommenced. The growth of a vancomycin-resistant, gram-positive coccus, later identified as *Leuconostoc citreum*, was obtained after 24 hours, with the following MIC values: vancomycin ≥ 500 $\mu\text{g/ml}$, penicillin 0.03 $\mu\text{g/ml}$, ampicillin 0.03 $\mu\text{g/ml}$, cefazolin 0.03 $\mu\text{g/ml}$, cefotaxime 0.03 $\mu\text{g/ml}$, imipenem 0.01 $\mu\text{g/ml}$, erythromycin 0.03 $\mu\text{g/ml}$, clindamycin 2 $\mu\text{g/ml}$, gentamicin 0.25 $\mu\text{g/ml}$, ciprofloxacin 2 $\mu\text{g/ml}$, rifampin 1 $\mu\text{g/ml}$ and fosfomycin 32 $\mu\text{g/ml}$. No tolerance to penicillin was detected. Three further blood cultures were obtained and treatment with i.v. penicillin was instituted. *Leuconostoc* was again isolated in this second set of blood cultures, as well as in the semiquantitative culture of the catheter tip and hub (> 15 cfu/plate). Cultures of the skin surrounding the insertion point of the catheter and of the parenteral nutrition fluid yielded no growth. The patient's temperature returned to normal after withdrawal of the catheter and 15 days' treatment with i.v. penicillin. Blood cultures obtained subsequently were found to be negative. Two years later the patient is asymptomatic and in a good clinical condition.

Case no. 2. A 72-year-old male smoker was admitted to the intensive care unit in October 1988 as a result of an acute myocardial infarct. While in hospital, he developed low cardiac output and acute pulmonary edema. On the ninth day in hospital he developed a high temperature which lasted 48 hours. His temperature subsided considerably after withdrawal of the central catheter, which unfortunately was not sent for culture. A microorganism, later identified as a *Leuconostoc* spp. with the same MIC and MBC values for

penicillin as the strain in case no. 1 was isolated in two of the three blood cultures obtained at the onset of the fever. No focus of infection was identified. As fever subsided after removal of the catheter, no antibiotic therapy was administered. The sudden death of the patient on the 12th day in hospital was not attributable to the bacteremia. Permission for autopsy was denied.

Microbiological Investigations. Microorganisms were identified as *Leuconostoc* spp. by the following criteria: gram-positive coccobacilli, resistance to vancomycin, no production of catalase, negative Voges-Proskauer test, production of gas from glucose in Mann, Rogosa and Sharpe broth (Oxoid, UK), non-deamination of arginine and negative pyrrolidonylarylamidase activity (2, 4, 13–18). The identification of the strain in case no. 1 was kindly confirmed by Dr. Facklam. The MICs of the antibiotics tested were determined by the broth microdilution method applying the NCCLS criteria (19), as were the MBC and tolerance. Catheters were processed for culture according to the semiquantitative method of Maki et al. (20). Hubs and swabs of skin surrounding the catheter insertion point were processed by semiquantitative techniques as described elsewhere (21, 22). The Bactec NR-660 (Johnston Laboratories, USA) was employed for blood cultures in our laboratory.

Discussion. In a literature search for the period 1980 to 1989 we were able to find 12 published reports of cases of bacteremia caused by *Leuconostoc* spp. We have only included in our review those cases in which the microbiological and clinical data necessary to confirm the identification and clinical significance of *Leuconostoc* were provided (9–11). Seven cases (5, 6, 9) were excluded on these grounds. One case with an isolate originally described as vancomycin resistant *Streptococcus sanguis* (23) was not included although it might very well have been a case of *Leuconostoc* infection (24). The remaining five cases, as well as our two patients, were included in the further analysis (Table 1).

Four of the seven patients were less than one year of age. All presented with underlying diseases, of which the most common was diarrhea related to gastrointestinal pathology.

Bacteremia was nosocomially acquired in six cases. In the remaining case endocarditis was suspected in a patient with pre-existing valve pathology, but could not be confirmed. Five patients had had previous staphylococcal bac-

Table 1: Clinical and microbiological characteristics of patients reported with bacteremia caused by *Leuconostoc* species.

Patient no.	Refer-ence	Age/Sex	Underlying disease	Acquisition	Previous infections	Prior vancomycin therapy	Intra-venous catheter	Source of isolation	Treatment	Clinical course	<i>Leuconostoc</i> species
1	(9)	53 y/f	alcoholism, encephalopathy	nosocomial	MRSE bacteremia	yes	yes	blood	penicillin	cure	<i>L. paramesenteroides</i>
2	(9)	2 m/m	anoxic, encephalopathy	nosocomial	pneumonia, MRSA bacteremia	yes	yes	blood	catheter withdrawal	cure ^a	<i>L. paramesenteroides</i>
3	(10)	2.5 m/f	premature birth, necrotizing colitis	nosocomial	Serratia and MRSE bacteremia	yes	yes	blood with MRSE, catheter tip and hub	clindamycin	cure	<i>Leuconostoc</i> sp.
4	(11)	1 m/m	necrotizing colitis	nosocomial	MRSE bacteremia	yes	yes	blood, catheter tip and hub	penicillin	cure	<i>L. mesenteroides</i>
5	(12)	64 y/f	mitral valve prolapse	community acquired	none	no	no	blood	penicillin + gentamicin	cure	<i>Leuconostoc</i> sp.
6	(present report)	7 m/m	malabsorption, monosaccharide intolerance	nosocomial	MRSE bacteremia	yes	yes	blood, catheter tip and hub	penicillin	cure	<i>Leuconostoc citreum</i>
7	(present report)	72 y/m	acute myocardial infarct, cardiac arrest	nosocomial	none	no	yes	blood	catheter withdrawal	cure ^b	<i>Leuconostoc</i> sp.

MRSA: methicillin-resistant *Staphylococcus aureus*. MRSE: methicillin-resistant *Staphylococcus epidermidis*.

^a Unrelated death two months later.

^b Unrelated death 3 days later.

teremia (*Staphylococcus epidermidis* in four cases and methicillin-resistant *Staphylococcus aureus* in one) and had been on or were still on treatment with vancomycin when *Leuconostoc* bacteremia was detected. In six patients intravenous catheters were considered to be the origin of the bacteremia.

The standard case of *Leuconostoc* bacteremia presented clinically as fever in a hospitalized patient, without shock, disseminated intravascular coagulation or other severe complications and with no clear portal of entry.

All seven strains were resistant to vancomycin (MIC ≥ 256 $\mu\text{g/ml}$). Susceptibility test results for other antimicrobials were available for five strains, of which the majority were sensitive to penicillin, with MICs between 0.03 and 1 $\mu\text{g/ml}$, although one tolerant strain was reported. The isolates were also sensitive to ampicillin, cefazolin, cefotaxime, imipenem, rifampicin, gentamicin and erythromycin. Three strains were sensitive to clindamycin.

Five patients received correct antibiotic treatment, in four cases with penicillin. One patient with infection caused by a penicillin-tolerant strain recovered in spite of being treated with this antibiotic. The remaining two patients received no antibiotic therapy, and catheter removal was sufficient for cure. Although two patients died in hospital, neither death could be attributed to the bacteremia.

It is only recently that *Leuconostoc*, a microorganism routinely used in industrial microbiology, has come to be considered a potential human pathogen (4). Occasional isolates from gastrostomy exudates (11, 25), peritoneal dialysis fluids (8) and others sources (7) have doubtful clinical significance. Even blood isolates cannot be routinely considered significant (5, 6, 9–12). In only five of the 12 cases of bacteremia which we were able to find in the medical literature was the pathogenic role of this microorganism unquestionable.

The incidence of *Leuconostoc* bacteremia is very low (2 of 709 significant cases of bacteremia in 1988 in our institution), although its possible confusion with *Streptococcus viridans* or *Enterococcus* when routine sensitivity studies are not performed may contribute to underestimation of its real importance.

The majority of patients with bacteremia caused by *Leuconostoc* spp. are premature babies hospitalized in intensive care units with diarrhea resulting from intestinal disorders. This may be due to

colonization of the newborn during labor, although *Leuconostoc* has only very occasionally been isolated from the vagina of healthy women (3). Another possible explanation is contamination of milk derivatives used in infant nutrition (11). The adults reported with *Leuconostoc* bacteremia were patients over 50 years of age in intensive care units who had indwelling intravenous catheters. Portals of entry for *Leuconostoc* bacteremia were either catheters (6 of 7 cases) or unknown (1 case). The most frequent clinical presentation was non-focal nosocomial fever in patients who either had been or who were still being treated with vancomycin.

Leuconostoc, in spite of being gram-positive, shows intrinsic, non-transferable resistance to vancomycin (26). This natural resistance is due to the production of cell wall peptides devoid of binding sites for vancomycin (D-alanyl-D-alanine) (1, 27). The production of extracellular substances which inactivate or destroy vancomycin has therefore been ruled out (26). As a result *Leuconostoc* behaves as a superinfection in patients being treated with vancomycin. The penicillins are adequate for treatment of *Leuconostoc* bacteremia. In all the cases of catheter related bacteremia analysed, the indwelling catheter was removed. We were unable to find any death unquestionably attributable to *Leuconostoc* bacteremia.

All gram-positive blood isolates should be tested routinely for vancomycin susceptibility and *Leuconostoc* spp. must be borne in mind when a vancomycin-resistant coccobacilli is detected. *Leuconostoc* spp. should be listed in the group of microorganisms producing bacteremia, and their presence should be specifically sought in children with central catheters and diarrhea who have previously been treated with vancomycin.

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Peritonitis with CDC Group IVc-2 Bacteria in a Patient on Continuous Ambulatory Peritoneal Dialysis

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A case of CDC group IVc-2 peritonitis in a patient on continuous ambulatory peritoneal dialysis (CAPD) is described. To the authors' knowledge, this is the first case reported of CAPD peritonitis in which a member of this unusual group of bacteria was isolated as the sole microorganism. As this microorganism is usually resistant to most antibiotics commonly used to treat peritonitis in patients on CAPD, microbiological investigations with identification and antimicrobial susceptibility tests are mandatory.

Human infections caused by bacteria of CDC group IVc-2 are rare. To our knowledge there are only three case reports dealing with infection caused by such microorganisms: two cases of septicemia (1, 2) and a third case of mixed infection with *Alcaligenes faecalis* and a CDC group IVc-2 organism in a patient on continuous ambulatory peritoneal dialysis (CAPD) (3). We present here the first case reported of peritonitis in which a member of CDC group IVc-2 was the sole microorganism isolated.

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