

## Septicemia Caused by Vancomycin-Resistant *Pediococcus acidilactici*

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**A case of septicemia caused by vancomycin-resistant *Pediococcus acidilactici* is discussed. This appears to be the first reported case of septicemia caused by this organism. The characteristics and antimicrobial susceptibilities of this organism are described.**

The genus *Pediococcus* consists of eight species of homofermentative lactic acid bacteria. Some have industrial importance in the food industry and as silage additives (7). With one exception without case details (2), these organisms have not been previously described as human pathogens. In one study, vancomycin-resistant pediococci were recovered from the feces of three healthy individuals (6); they appear to be a component of normal (fecal) flora (1).

We report the isolation of *Pediococcus acidilactici* from multiple blood cultures taken from a leukemic patient with a septicemic illness.

**Case report.** A 53-year-old farm laborer was referred to Sir Charles Gairdner Hospital, Nedlands, Western Australia, Australia, with a history suggesting acute leukemia. For 1 month, he had experienced recurrent skin infections, shortness of breath on exertion, easy bruising, and finally, an outbreak of herpes labialis. He experienced a weight loss of approximately 4 kg. His medical history was unremarkable, and he was taking no medications. He smoked 5 to 10 cigarettes and consumed approximately 20 g of alcohol daily.

Examination upon admission revealed lymphadenopathy, herpes labialis, a carbuncle on the dorsum of the right hand, and a deep ulcer on the buccal surface of the left upper lip. The patient was not in shock and had a temperature of 37.9°C. He did not have hepatosplenomegaly, skin deposits, gingival hyperplasia, petechiae, or neurological deficits. His respiratory and cardiovascular systems were normal. His leukocyte count was  $34.3 \times 10^9$ /liter, with 83% myeloblasts, 8.8 g of hemoglobin per dl, and a platelet count of  $20 \times 10^9$ /liter. A bone marrow aspirate was hypercellular, with over 90% of nucleated cells being poorly differentiated blasts. The findings were consistent with acute myeloblastic leukemia (type M1 in the FAB classification).

Intravenous empiric therapy with vancomycin (500 mg four times a day) and ceftazidime (1 g three times a day) was commenced. He was given oral acyclovir (1 g daily) in divided doses, allopurinol (300 mg daily), chlorhexidine sachets, and nystatin lozenges.

On day 3 after admission, intravenous metronidazole (500 mg three times a day) was added to the treatment, since the patient developed a tender swelling at the left angle of the jaw.

By day 6, fever persisted, with a rise in the absolute blast cell count from  $28.5 \times 10^9$  to  $49.8 \times 10^9$ /liter. A Groshong central venous catheter was inserted, and the patient re-

ceived cytosine arabinoside (170 mg per day) for 7 days and daunorubicin (78 mg per day) for 3 days. His temperature continued to spike as high as 40.5°C, and another 16 blood cultures (8 aerobic and 8 anaerobic) were negative. On day 14 after the commencement of chemotherapy, a gram-positive coccus was isolated from eight blood culture bottles (four aerobic and four anaerobic BACTEC NR660 bottles; Johnston Laboratories, Inc., Towson, Md.). This organism was provisionally identified as *Streptococcus equinus*; it was noted to be resistant to vancomycin. Vancomycin treatment was ceased, and benzylpenicillin (1.2 g intravenously four times a day) treatment was begun. Ceftazidime and metronidazole treatment was continued. Tobramycin (80 mg three times a day) treatment was commenced. Over the next 5 days, there was a clinical response with resolution of fever. Antibiotic treatment was then ceased.

By the start of week 5, after another episode of septicemia caused, on this occasion, by *Streptococcus sanguis*, there was recovery of bone marrow function and he was allowed home. After a third cycle of chemotherapy, the leukemia was in remission.

**Microbiological findings.** The organism grew both aerobically and anaerobically on 5% horse blood agar after overnight incubation in 10% CO<sub>2</sub>. Gram stains of both plate and thioglycolate broth cultures revealed gram-positive cocci in pairs, tetrads, and clusters. The organism grew at a range of temperatures from 25 to 50°C. It also grew on an acidic medium, Rogosa agar (Oxoid Limited, Basingstoke, United Kingdom). Catalase and oxidase reactions were negative. Biochemical tests were performed by the methods of Facklam et al. (3) and are shown in Table 1. In addition, a positive reaction was obtained with group D streptococcal antisera by using Streptex grouping (Wellcome Reagents Div., Burroughs Wellcome Co., Research Triangle Park, N.C.). The organism was identified as *S. equinus* by the AutoMicrobic system (Vitek Systems, Inc., Hazelwood, Mo.). Disk diffusion susceptibility testing on blood-supplemented Mueller-Hinton agar showed the organism to be susceptible to penicillin, amoxicillin, tetracycline, and erythromycin. It was resistant to vancomycin and teicoplanin but was susceptible to daptomycin (LY146032). Broth macrodilution MICs of vancomycin and teicoplanin were both in excess of 256 mg/liter.

**Discussion.** Vancomycin resistance in gram-positive bacteria is fortunately a rare phenomenon but can be expected to increase. Resistance has been reported among enterococci, leuconostocs, lactobacilli, and staphylococci, in addi-

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TABLE 1. Biochemical reactions of *Pediococcus acidilactici*

Biochemical test	Result
Acidification of:	
Glucose .....	+
Arabinose .....	+
Ribose .....	+
Xylose .....	+
Rhamnose .....	+
Lactose .....	-
Maltose .....	-
Sucrose .....	-
Starch .....	-
Mannitol .....	-
Sorbitol .....	-
Hippurate hydrolysis .....	+
Arginine deamination .....	+
Voges-Proskauer .....	-
Bile-esculin .....	+
Pyrridonylarylamidase .....	-
Leucine aminopeptidase .....	+
$\gamma$ -Galactosidase .....	+
Alkaline phosphatase .....	-
Nitrate .....	-
Urea hydrolysis .....	-
Motility .....	-
Growth in 6.5% NaCl .....	+

tion to pediococci (5, 6, 8; K. L. Ruoff, Clin. Microbiol. Newsl. 11:1-4, 1989). We have also noted almost universal resistance in *Nocardia* spp. and *Erysipelothrix rhusiopathiae*. Resistance among streptococci probably does not occur, since earlier reports may represent misidentifications (C. Thornsberry and R. R. Facklam, Antimicrob. Newsl. 1:63-64, 1984). Over a 2-year period, we have encountered blood culture isolates showing vancomycin resistance from eight patients. Besides the case presented here, four patients had septicemias with lactobacilli and one patient each had *Enterococcus faecium*, *Leuconostoc mesenteroides*, and *E. rhusiopathiae* (4; C. L. Golledge and J. M. Heywood, Program Abstr. Aust. Soc. Microbiol. Conf., abstr. no. 26.1, p. 382, 1989; C. L. Golledge, Clin. Microbiol. Newsl. 11:29-30, 1989).

Pediococci appear almost universally resistant to vancomycin. Four of five strains we tested were highly resistant to vancomycin, and the fifth strain had a vancomycin MIC of 8 mg/liter. All strains were susceptible to daptomycin.

In the cases we have encountered, both the leuconostoc and the pediococcus would have been misidentified as streptococci if we had not been aware of the significance of vancomycin resistance. The identification of pediococci as *S. equinus* has been previously reported (Ruoff, Clin. Microbiol. Newsl.). However, *S. equinus* is vancomycin susceptible and does not deaminate arginine (3).

To confirm an organism as a *Pediococcus* sp., a Gram stain is useful. Coccoid cellular arrangements in clusters and tetrads are consistently observed. Gas is not produced from glucose, a reaction with group D streptococcal antisera is usually seen, and the bile-esculin reaction is positive. In addition, there is a negative test reaction for pyrrolidonylarylamidase activity and a positive reaction for leucine aminopeptidase. Growth is variable in 6.5% NaCl, and the organism grows at 45°C. The lack of acidification of maltose and a negative Voges-Proskauer test result confirm this organism to be *P. acidilactici* and not another member of the *Pediococcus* genus. In addition, it would have been possible to identify this organism as an enterococcus because of its reaction with group D antisera, bile-esculin positivity, and growth in 6.5% NaCl. The negative test for pyrrolidonylarylamidase activity and lack of acidification of mannitol exclude this possibility.

There appears to be little doubt that pediococci are rare clinical isolates and that these organisms are opportunistic pathogens. Nevertheless, it is possible that infections with these organisms have been missed in the past. With the widespread use of vancomycin and increasing reports of resistance, coupled with the value of vancomycin resistance as a screening test for these unusual organisms, routine susceptibility testing of all gram-positive isolates against vancomycin is warranted. This report underlines the importance of the accurate identification of organisms found to be vancomycin resistant.

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