

## Meningitis in a Neonate Caused by *Leuconostoc* sp.

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**A case of meningitis in a neonate caused by vancomycin-resistant *Leuconostoc mesenteroides* is presented. This case was complicated by severe ventriculitis and was ultimately fatal. Infection with *Leuconostoc* spp. is rare but should be suspected when vancomycin-resistant organisms resembling streptococci are isolated. Previous reports of this infection are reviewed.**

*Leuconostoc* spp., although rarely pathogenic in humans, have recently been reported as causing serious infections (1, 2, 6, 7, 9, 11). We describe a neonate with meningitis caused by this organism and review previously reported cases.

**Case report.** A 1-month-old female infant presented with a 2-day history of poor feeding. She was born at term with a weight of 2.34 kg (small for gestational age). Hirschsprung's disease was diagnosed during the first week of life, and a defunctioning colostomy was performed. The infant had an uneventful postoperative recovery and was discharged well 1 week prior to the present admission. She had been fed on a "humanized" infant formula (S26-Wyeth) since birth. Examination revealed a wasted, irritable infant weighing 2 kg. The anterior fontanel was bulging, the muscular tone was increased, and the reflexes were brisk. A colostomy was noted. No other abnormalities were detected.

Cerebrospinal fluid (CSF) obtained on admission was turbid, with  $1,040 \times 10^6$  neutrophils and  $190 \times 10^6$  lymphocytes per liter, 7.3 g of protein per liter, and 12.1 mmol of glucose per liter (blood glucose, 23.6 mmol/liter). No bacteria were observed on Gram staining of the CSF. Other laboratory results were as follows: hemoglobin, 8.0 g/dl; leukocytes,  $16.1 \times 10^9$ /liter; platelets,  $425 \times 10^9$ /liter; total serum protein, 54 g/liter (albumin, 34 g/liter; globulin, 20 g/liter); and normal liver enzymes.

Treatment with intravenous penicillin (high dose) and cefotaxime was started. Culture of the CSF yielded gram-positive cocci resembling streptococci. However, because this organism was resistant to vancomycin further identification was done (see below).

Three days after admission, the infant developed generalized convulsions and phenobarbital was commenced. There were no further convulsions. Cranial ultrasonography at this time showed marked hydrocephalus involving all the ventricles. No abscess, subdural effusion, or midline shift was observed. The condition of the infant did not improve, and a computerized tomography scan revealed hydrocephalus with ventriculitis. Turbid ventricular fluid was obtained via the anterior fontanel and contained  $495 \times 10^6$  neutrophils per liter, protein of 6.5 g/liter, and glucose of  $<1$  mmol/liter. Gram-positive cocci were observed but did not grow on culture. Chloramphenicol was added, and daily ventricular taps were commenced with simultaneous instillation of intraventricular gentamicin (1 mg). Two days later, organisms were again observed. At this time the CSF was bactericidal for the organism at a dilution of 1:64. Repeat CSF (ventric-

ular) examinations showed a progressive increase in neutrophil count and protein concentration, but organisms were not observed again. CSF bactericidal activity was now demonstrated to occur at a dilution of 1:2,048. Repeat cranial sonography showed pus casts in the ventricles, and the infant died shortly afterwards.

Neutrophil function tests revealed minor nonspecific defects suggestive of overwhelming bacterial infection. Serum immunoglobulin concentrations were normal for age.

**Microbiological identification.** The CSF isolate was identified as *Leuconostoc* species on the basis of the following findings: (i) gas produced from glucose in MRS broth (2a); (ii) catalase and oxidase negativity; (iii) esculin hydrolysis, nitrite reduction, and gelatin liquefaction positivity; (iv) fermentation of glucose, sucrose, maltose, ribose, D-xylose, salicin, cellobiose, L-arabinose, galactose, and N-acetylglucosamine; (v) nonfermentation of mannitol, dulcitol, L-xylose, sorbitol, inositol, inulin, and L-sorbose; (vi) streptococcal group antigen negativity; and (vii) growth in 6.5% NaCl at 10°C. The organism was identified as *Leuconostoc mesenteroides* according to the reactions as described by Facklam et al. (3).

**Antibiotic susceptibility.** MICs were determined by microtiter broth dilution with the following results (in mg/liter): vancomycin,  $>128$ ; fucidic acid,  $>128$ ; trimethoprim,  $>64$ ; penicillin, 0.06; erythromycin,  $<0.06$ ; chloramphenicol, 8; clindamycin, 8; cefazolin, 4; and gentamicin, 0.12.

*Leuconostoc* are coccoid gram-positive facultative anaerobes that rarely infect humans. They are commonly found on plants and less often in dairy products. *Leuconostoc oenos* is recovered from wine (4). Vancomycin-resistant gram-positive cocci (including *Leuconostoc* spp.) have been isolated from the stools of children, thus raising the possibility that the gastrointestinal tract can act as a site of colonization and source of infection (5). Rubin et al. isolated *Leuconostoc lactis* from rehydrated infant formula (9). Unfortunately, the gastrointestinal tract and infant formula as possible sources of infection were not investigated in this case.

*Leuconostoc* spp. may be nonhemolytic (4) or alpha-hemolytic (8) and may be mistaken for viridans group streptococci or *Streptococcus pneumoniae*. However, unlike streptococci they are highly resistant to vancomycin and produce gas during glucose fermentation (8). *Lactobacillus* spp. may also be confused with *leuconostoc*s (4, 8).

This report describes a neonate who developed meningitis at 1 month of age. Meningitis in a 16-year-old caused by *Leuconostoc* sp. was reported from South Africa (2), but this is thought to be the first description of neonatal meningitis due to a *leuconostoc* (in this instance, *L. mesenteroides*).

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TABLE 1. Clinical details of reported infections due to *Leuconostoc* spp.

Patient no. (reference)	Age	Site(s) of infection	Predisposing factor(s) <sup>a</sup>	Outcome
1 (1)	36 yr	Blood	SLE on steroids	Death
2 (1)	40 yr	Blood	Brain hemorrhage, postoperative pneumonia	Recovery
3 (2)	16 yr	CSF	None	Recovery
4 (7)	53 yr	Blood	Multiple organ derangements, i.v. catheter	Recovery
5 (7)	78 yr	Blood	Hemodialysis	Recovery
6 (7)	2.5 mo	Blood	CNS anoxia, multiple infections, i.v. catheter	Death
7 (9)	6 mo	Blood, catheter hub, gastric fluid	i.v. catheter, long-term parenteral nutrition	Recovery
8 (6)	2 mo	Blood and catheter tip	Premature on long-term parenteral nutrition	Recovery
9 (11)	58 yr	Tooth abscess	None	Recovery
10 <sup>b</sup>	1 mo	CSF	Neonate	Death

<sup>a</sup> SLE, Systemic lupus erythematosus; i.v., intravenous; CNS, central nervous system.

<sup>b</sup> Present case.

This case was complicated by the development of severe ventriculitis which did not respond to intravenous penicillin and intraventricular gentamicin, and the baby died.

Since organisms persisted in ventricular fluid despite adequate antibiotic levels and the presence of numerous leukocytes, a defect in leukocyte killing was suspected. However, no such defect could be demonstrated. The aggressive nature of the illness in this case may have been related to the relative immaturity of the neonatal immune system.

Published reports (including the present case) of human infections due to leuconostocs are summarized in Table 1. Four of the ten patients had indwelling intravenous catheters, and three others were compromised in other ways. It is thus evident that breakdown in host defenses is an important predisposing factor. In addition to these cases, a vancomycin-resistant viridans group streptococcus reported by Shlaes et al. (10) may actually have been a *Leuconostoc* sp. (8).

This report is further evidence that, although rarely pathogenic, leuconostocs may cause severe infection in humans.

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