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Catheter Related *Leuconostoc Mesenteroides* Bacteremia: A Rare Case and Review of the Literature

Kateter İlişkili *Leuconostoc Mesenteroides* Bakteriyemisi: Nadir Bir Olgu ve Literatürün Derlenmesi

Adem Karbuz[1], Bilge Aldemir Kocabaş[1], Aytaç Yalman[2], Zarife Kuloğlu[2], Ahmet Derya Aysev[3], Ergin Çiftçi[1], Erdal İnce[1]

[1]*Ankara University Faculty of Medicine, Department of Pediatrics, Division of Pediatric Infectious Diseases, Ankara, Turkey*
[2]*Ankara University Faculty of Medicine, Department of Pediatrics, Ankara, Turkey*
[3]*Ankara University Faculty of Medicine, Department of Clinical Microbiology, Ankara, Turkey*

ABSTRACT

Herein we report the successful treatment of catheter related blood stream infections due to *Leuconostoc mesenteroides* with antibiotic lock therapy in addition to systemic treatment. With our case, we have shown that in the presence of catheter related blood stream infections, antibiotic lock therapy can be used as a therapeutic option to get successful results if the catheter cannot be removed or there are still positive cultures despite the systemic antibiotic therapy.

Keywords: *Leuconostoc mesenteroides*, catheter related bacteremia, antibiotic lock therapy

ÖZ

Leuconostoc mesenteroides'e bağlı kateter ilişkili kan akımı enfeksiyonunun sistemik tedaviye ilaveten antibiyotik kilit tedavisi ile başarılı bir şekilde tedavi süreci anlatıldı. Sunulan olguyla kateter ilişkili kan akımı enfeksiyonu varlığında eğer kateter çıkartılamıyor ve sistemik antibiyotik tedavisine rağmen üreme devam ediyorsa antibiyotik kilit tedavisinin uygulanabileceği ve başarılı sonuç alınabileceği gösterildi.

Anahtar Kelimeler: *Leuconostoc mesenteroides*, kateter ilişkili enfeksiyon, antibiyotik kilit tedavisi

Introduction

Advances in the field of microbiology and awareness among the microbiologists led to an increase in the rate of identification of rare opportunistic microorganisms in humans. *Leuconostoc* species are catalase negative, facultative anaerobic gram positive cocci configured in doubles or chains. They are usually found in plants, dairy products, wine and food. They are initially believed to be a member of the flora of vagina and gastrointestinal system (1,2). In recent years, many case reports of serious infections led to an increased awareness and focus on risk factors, pathogeneticity and treatment options.

This case report documents the successful treatment of catheter associated blood stream infection due to *Leuconostoc* bacteria with antibiotic lock treatment in addition to systemic antibiotic treatment. This is a novel approach in cases where catheter removal is not an option because of

Address for Correspondence/Yazışma Adresi
Adem Karbuz MD, Ankara University Faculty of Medicine, Department of Pediatrics, Division of Pediatric Infectious Diseases, Ankara, Turkey
Phone: +90 506 408 03 53 E-mail: karbuzadem@hotmail.com
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the lack of alternative intravenous line. To our knowledge, it is the first known report of *Leuconostoc mesenteroides* bacteremia successfully treated with antibiotic lock therapy.

Case Report

A fifty-day-old girl was admitted to pediatric gastroenterology department with chronic diarrhea. She had complaints of diarrhea and vomiting for two weeks. Following diagnostic endoscopy, she suffered from a duodenum perforation. A central catheter was placed at the surgery. After the operation, piperacillin-tazobactam, teicoplanin and fluconazole were given as an empirical therapy. Total parenteral nutrition (TPN) was initiated. Her fever began five days later from the cessation of empirical antibiotic therapy. Laboratory workup revealed white blood cell count 13.700/mm^3, hemoglobin 9.8 g/dL, platelet count 328.000/mm^3, C-reactive protein: 22 mg/dL. Blood cultures were taken, empirical fluconazole and cefoperazone-sulbactam were initiated. As fever continued, teicoplanin was added on the second day. Amikacin was added on the third day because her appearance became worsened. Although initial blood cultures remained sterile, blood cultures taken on the third day of the therapy were positive for gram positive cocci. She had an intractable fever exceeding 39 °C. *Leuconostoc mesenteroides* were identified in addition to coagulase negative *Staphylococcus* on the seventh day of therapy. The signal for growth of *Leuconostoc* was detected at 5th and 13th hours from the catheter culture and peripheral vein culture, respectively. Teicoplanin was discontinued on the 6th day and high dose linezolid and ampicilline were initiated. Catheter lock therapy was planned but the central line was accidentally removed. As no other vascular access could be obtained, another central catheter was placed despite ongoing bacteremia. Echocardiography was negative for valvular vegetations. Abdominal ultrasonography revealed ascites. Cultures of peripheral blood and catheter remained positive for *Leuconostoc*. The signal for growth of *Leuconostoc* was detected from the catheter culture and the peripheral vein culture at 13th and 28th hours, respectively. Antibiotic lock therapy was re-initiated on the 12th day of fever. On the third day of antibiotic lock therapy, her fever resolved, and cultures remained sterile. Rectal cultures were positive for *Escherichia coli*. After systemic antibiotherapy for three weeks, antibiotic lock therapy for 2 weeks and full enteral feeding, she was discharged from the hospital.

Discussion

Leuconostoc spp. is a member of *Streptococcaceae* family. It is not an easily recognized microorganism by routine biochemistry and phenotypical identification. As it is a non-hemolytic or alfa-hemolytic gram positive coccus on sheep agar, it may be mistaken for *Enterococcus* or *Streptococcus* (3). Like *Enterococci* it may reproduce in 6.5% NaCl and hydrolysis esculin in the presence of bile. *Leuconostoc* species are incapable of producing leucine aminopeptidase and pyrrolidonyl arylamidase. CO_2 formation with glucose are distinctive properties while not a part of routine investigations in many microbiology labs. Antibiotic sensitivity tests are important for identification. *Leuconostoc* species are naturally glycopeptide resistant (1). In our case, blood cultures revealed non-hemolytic gram positive cocci, forming short chains mostly in doubles which were initially thought to be *Streptocci*. Antibiotic sensitivity test showed sensitivity to ampicillin and penicillin but resistance to vancomycin, it was suspected from *Leuconostoc* species. A verification was performed using BD phoenix 100 version 6.01A. Result was 99% consistent with *Leuconostoc mesenteroides spp. mesenteroides*.

Leuconostoc species were not considered as pathogens for humans until early eighties. The first report as human pathogen was by Buu-Hoi et al. (4) in 1985. Two cases with blood cultures which had gram positive cocci resistant to vancomycin were reported. They were initially identified as *Streptococci* by API 20 Strep system but gas production from glucose and fermentation status of various carbohydrates led to the identification of *Leuconostoc* species (4). *Leuconostoc* has been accepted as the etiologic agent for bacteremia, sepsis, catheter related blood stream infection, meningitis, endocarditis, brain and liver abscess, osteomyelitis, pulmonary and nosocomial infections (1,3,5-9). Sixty percent of *Leuconostoc* case reports between 1985 and 1996 were of children (10). Most of the patients presenting with *Leuconostoc* were immunocompromised patients (malignancy, liver transplantation, chemotherapy, immunosuppression) (10-13). However, some patients with *Leuconostoc* infection were immunocompetent (14). Other risk factors among published reports were gastrointestinal disease, prior vancomycin therapy, surgery distrupting gastrointestinal mucosal integrity, TPN usage, central venous line, prematurity (1,3,10,13,15).

Immunologic workup revealed no immune deficiency in our case. Chronic diarrhea, gastrointestinal surgery, vancomycin therapy, central venous catheter and TPN administration were important risk factors for *Leuconostoc* infection.

Even though *Leuconostoc* species are isolated from vaginal and fecal samples, they are not considered to be normal flora members. Site of entry is not clear in infections due to *Leuconostoc* species. Few reports speculate that the site of entry can be skin (16,17). Co-infection with coagulase negative staphylococci raise the suspicion of entry through skin (3,10,16). As most cases of *Leuconostoc* infection have central catheter, speculations about disrupted skin integrity during catheter insertion is the main cause (3,16,17). Others speculate that gastrointestinal system is another entry site. They state that when the gastrointestinal system is colonized with *Leuconostoc*, translocation occurs (3,15,16). In another report, 35 percent of cases have polymicrobial etiology, so intra-abdominal source may be suspected (13). Moreover, *Leuconostoc* species are isolated from infant formula, various foods, gastric aspirates, gastrostomy tubes

and these support the idea of gastrointestinal entry (15,18). Apart from that, a report by Bou et al. (6) documents TPN as the source of nosocomial *Leuconostoc* infections. It is clear that in our case there are multiple risk factors. It is hardly possible to tell which factor has the leading role, but it may be speculated that gastrointestinal route is more probable case due to chronic diarrhea. Simultaneous resolution of diarrhea and infection supports this hypothesis.

Management of *Leuconostoc* infections consists of appropriate antibiotic therapy and removal of infection source (catheter removal, draining of abscess) (3). The most preferred antibiotic for *Leuconostoc* infections is penicillin with or without gentamicin. Minimum inhibitory concentration value of penicillin is higher than *Streptococci* mandating a higher dose or combination with an aminoglycoside (3,10). In published reports, *Leuconostoc* infections are successfully treated by ampicillin, cefotaxime, carbapenem, clindamycin, erythromycin and recently by daptomycin (1,3,19). The characteristics of pediatric patients who have gastrointestinal disease with *Leuconostoc* bacteremia is shown in Table I (3).

Management of catheter related bacteremia is not clear. In most cases of catheter related bacteremia, catheter removal has been required (10,15). In three cases, bacteremia was resolved without antibiotic treatment following catheter removal (10,16,17). Guideline for catheter related blood stream infections does not contain information about *Leuconostoc* (20). No information regarding biofilm formation of *Leuconostoc* was found. Former reports show a tendency towards catheter removal for the control of infection. In our case, linezolid and ampicillin therapy was initiated following the identification of *Leuconostoc*. Vascular access problem mandated antibiotic lock therapy but the central line was accidentally removed. Another central catheter was inserted immediately. Blood cultures remained positive and the second catheter was also colonized with *Leuconostoc*. Due to catheter related blood stream infection, positive blood cultures and persistence of systemic signs required antibiotic lock therapy. The combined lock solution was prepared by mixing ampicillin 10 mg/mL and heparin 5000 units/mL for antibiotic lock therapy. Then, the solution was administered into the lumen of the catheter every 12 hours. Following lock therapy, blood cultures remained sterile and clinical signs improved. Systemic therapy with linezolid and ampicillin was continued for 21 days, while lock therapy lasted for 12 days. Three months follow-up revealed no problems.

Leuconostoc species should be kept in mind in cases of vancomycin resistant gram positive infections. Even though they are rare pathogens for humans, they may cause serious infections. In cases of catheter related blood stream infections where systemic antibiotic treatment fails and

Table I. The characteristics of pediatric patients who have gastrointestinal disease with *Leuconostoc* bacteremia (3)

C	Age	Sex	Primary disease	TPN	CVC	Previously vancomycin therapy	Treatment	Line removal
1	6 months	M	Gastroschisis and bowel infarction	+	+	-	Ampicillin (14 days)	No
2	3 years 6 months	F	Gastroschisis	+	+	Unknown	Ampicillin (14 days)	Yes (venous thrombosis)
3	6 months	M	Necrotizing enterocolitis	+	+	Unknown	Penicillin (14 days)	Yes
4	11 years	F	Midgut volvulus and congenital malrotation	+	+	-	Ampicillin and gentamicin (14 days)	Yes
5	8 months	F	Gastroschisis	+	+	-	Imipenem (14 days)	Yes
6	2 years	F	Jejunal atresia	+	+	+	Imipenem (17 days)	Yes
7	2 months	F	Necrotizing enterocolitis	-	+	+	Vancomycin clindamycin(14 days)	Yes
8	1 months	M	Necrotizing enterocolitis	+	+	+	Penicillin (14 days)	No
9	9 months	F	Jejunal atresia	+	+		Ampicillin + gentamicin (10 days)	No
10	20 months	F	Necrotizing enterocolitis	+	+	+	Amoxicillin (14 days)	Yes
11	4 years	M	Malrotation and volvulus	+	+	+	Amoxicillin (14 days)	No
12	7 months	F	Gastroschisis, small bowel and colonic atresia	+	+	+	Ampicillin + gentamicin	Yes
13	13 months	F	Gastroschisis, jejunalatresia	+	+	+	Penicillin (14 days)	Yes
14	10 months	M	Necrotizing enterocolitis	+	+	+	Ampicillin + gentamicin	No
15	1 years	F	Jejunal atresia	+	+	+	Vancomycin + cefotaxime + metronidazole	Yes
16	8 months	F	Hirschsprung and intestinal obstruction	+	+	+	Clindamycin + amikacin (16 days)	Yes
PC	1 months	F	Chronic diarrhea	+	+	+	Ampicillin + linezolid (21 days) andampicillin lock therapy (14 days)	No

TPN: Total parenteral nutrition, CVC: Central venous catheter, C: Cases, PC: Present case, F: Female, M: Male

catheter removal is impossible, antibiotic lock therapy may be a therapeutic option.

Ethics

Informed Consent: *Retrospective study.*
Peer-review: Externally peer-reviewed.

Authorship Contributions

Medical Practices: Adem Karbuz, Bilge Aldemir Kocabaş, Aytaç Yalman, Zarife Kuloğlu, Ahmet Derya Aysev, Erdal İnce, Concept: Adem Karbuz, Design: Adem Karbuz, Data Collection or Processing: Adem Karbuz, Bilge Aldemir Kocabaş, Aytaç Yalman, Analysis or Interpretation: Ergin Çiftçi, Literature Search: Adem Karbuz, Writing: Adem Karbuz.

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