A Case of Bacterial Meningitis Due to Vancomycin Resistant *Enterococcus Casseliflavus* in a Nursling Child

Bir Süt Çocuğunda Vankomisine Dirençli *Enterococcus Casseliflavus'a* Bağlı Bakteriyel Menenjit vakası

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Abstract
Enterococcus casseliflavus is a rare pathogen that plays a role in various infections. It causes infections such as sepsis in humans. In adults, these are usually vancomycin resistant cases. We present a rare case of vancomycin-resistant *E. casseliflavus* meningitis in a 17-months-old girl who has been successfully treated with linezolid. The patient completely recovered after fourteen days of linezolid treatment. Vancomycin-resistant *E. casseliflavus* may be a potential pathogenic cause of meningitis in children with good clinical outcome by linezolid treatment. Linezolid therapy should be considered in children cases when vancomycin therapy failed.

Keywords: *Enterococcus casseliflavus*, Meningitis, Pediatrics

Öz
Enterococcus casseliflavus çeşitli enfeksiyonlarda rol oynayan nadir görülen bir patojendir. İnsanlarda sepsis gibi enfeksionlara yol açar ve bunlar genellikle erişkinlerde görülen vankomisin tedavisine direnç gösterebilen vakalardır. Biz bu raporda, 17 aylık bir kız çocuğunda linezolid ile başarılı bir şekilde tedavi edilen ve nadir görülen vankomisin dirençli bir *E. casseliflavus* menenjiti olgusunu sunmaktayız. Hasta ondört günlük linezolid tedavisi ile düzeldi. Vankomisin dirençli *E. casseliflavus* çocuklarda görülen menejitlerin potansiyel patojen bir nedeni olabilir ve tedavide linezolid kullanımı ile iyi klinik sonuçlar alınmaktadır. Çocuk hastalarda vankomisin tedavisine cevap alınamayan durumlarda, vankomisin dirençli *E. casseliflavus* düşünülmelidir.

Anahtar kelimeler: *Enterococcus casseliflavus*, Meninjit, Pediatri

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Geliş tarihi / Received:
26/03/2018

Kabul tarihi / Accepted:
13/04/2018

INTRODUCTION

Enterococcus spp. are primarily found in the water, soil and food stuffs. *Enterococcus fecalis* and *Enterococcus faecium* are main human pathogens (1,2). Other enterococcal species such as *E. casseliflavus* and *E. gallinarum* are motile enterococci causing serious invasive infections in 1-2% of all enterococcal infections especially in older patients (2,3). Despite its rarity, the importance of this pathogen has increased recently since it was implicated in infections in immunocompromised patients, and it displays intrinsic low level resistance to vanocomysin and some strains show high level resistance to aminoglycosides (4). The aim of the present report is to present a case of meningitis caused by *E. casseliflavus* in a child.

CASE REPORT

A 17 months old female nursling child with fever, coughing and irritability was administered to Sanliurfa Pediatric Hospital, Sanliurfa, Turkey. There was no history of previous illness or an underlying disease. Physical examination revealed fever (38.2 ºC), pulse rate 128/min, blood pressure 110/75 mmHg and respiratory rate 24/min. Oropharynx was hyperemic with oral aphts and gingivitis.

Laboratory examination showed haemoglobin (HB) 10 g/dL, haematocrit of 32.3 %, white blood cell (WBC) count 16100/mm^3 (predominance of neutrophils 72% and 28% other leukocytes) platelet count 244000/mm^3, ESR 20 mm/h and C-reactive protein (CRP) 130 mg/L. Serum biochemical tests were within normal limits. Combined therapy of ceftriaxone and amikacin was started empirically and continued for 4 days. Oral lesions improved after the antibiotic therapy. However, body temperature and CRP remained high. So, lumbar puncture was performed on the 4^{th} day. Examination of CSF revealed WBC count 1600 cells/ml (95% polymorphonuclear leukocytes PNL), protein level 1438 mg/L (normally 150-450 mg/L) and glucose concentration 14.6 mg/dL (simultaneous blood glucose 140 mg/dL). Direct Gram stain of CSF showed Gram positive cocci and PNL. The general condition of the patient was deteriorating. Therefore, we discontinued the treatment and a new empirical antibiotic treatment was started with vancomycin and imipenem. The organism yielded yellow colonies on both blood and Muller-Hinton agar. It was also positive for bile-esculin test and growth in 6.5% NaCl. The organism was identified as *E. casseliflavus* using Vitek 2 Compact (BioMerieux, France). The isolate was sensitive to ampicillin (MIC,2µg/ml), erythromycin (MIC,0.5µg/ml), imipenem (MIC,1µg/ml), ciprofloxacin (MIC,0.5µg/ml), moxifloxacin (MIC,0.25µg/ml), teicoplanin (MIC,0.5µg/ml) and gentamicin (MIC,0.1µg/ml). It was resistant to clindamycin (MIC,8µg/ml), trimethoprim/sulfamethoxazole (MIC,10µg/ml), tetracycline (MIC,16µg/ml), high dose of streptomycin (MIC,2000µg/ml), and vancomycin (MIC,4µg/ml).

Accordingly to antimicrobaial test report, combined vancomycin and imipenem was discontinued after three days post therapy. Sulbactam ampicillin was started at a dose of (3x100 mg/kg/day). Fever was still present and no improvement in patient's condition was seen within 48 hours of treatment. Thereafter, treatment was changed to intravenous linezolid (10 mg/kg/day). Forty eight hours after therapy, fever disappeared and the patient's general condition improved. On the 4th day of linezolid treatment, blood WBC count declined to 10000 cells /mL and CRP was 5.6mg/dL. Lumber puncture was repeated and it showed no leukocytes and absence of bacterial growth. Other CSF values were normal. Therapy continued daily for 14 days. The patient recovered completely and discharged from the hospital.

DISCUSSION

Enterococcal meningitis is an uncommon disease. *E. fecalis* and *E. faecium* are responsible for most of enterococcal infections in humans and rarely involved in bacterial meningitis. They account for 0.3–4% of the reported cases of bacterial meningitis (5). Motile enterococci such as *E. gallinarum* and *E. casseliflavus* are unusual etiological agents of bacterial meningitis. Several studies have demonstrated that motile enterococci colonize the gastrointestinal tracts of both hospitalized individuals and nonhospitalized healthy ones (6). They are usually implicated in bacteremia cases (2,6-8). They are naturally resistant to vancomycin and best treated with linezolid and daptomycin (3,6). Review the literature, there were three cases of *E. gallinarum* meningitis and two cases of *E. casseliflavus* meningitis (9,10). The first case of *E. casseliflavus* meningitis was in an elderly woman. Our case report describes the clinical features and outcome of *E. casseliflavus* in pediatric meningitis. Our patient was a hospitalized child in whom a tentative diagnosis of pneumonia was made on the hospitalization day. On the hospitalization day 4, his condition deteriorated again. *E. casseliflavus* was isolated from the CSF. Although there was no clear focus for *E. casseliflavus* in our case, we believe that the source of infection could have been the patient's own gastrointestinal flora.

Antimicrobial therapy with various agents such as cephalosporins and vancomycin may play a role in increasing colonization with these organisms (11). However, treatment should be regulated according to the results of sensitivity tests. VanC genotype is responsible for low intrinsic resistance to vancomycin in *E. casseliflavus* and VanC-2/3 ligase is specific for it (12,13). A case of enterococcal meningitis caused by *E. casseliflavus* was successfully treated with meropenem and ampicillin-sulbactam (9). Similar to other studies, our isolate was also susceptible to ampicillin. Ampicillin-sulbactam therapy was administered. Lack of clinical improvement or poor response as well as the patient's clinical deterioration, prompted us to change the treatment to linezolid, the first member of oxazolidone The difficulty in treating *E. casseliflavus* meningitis may be due to drug kinetics and microbial drug resistance. On the second day after the initiation of treatment, both the patient's clinical and laboratory findings gradually improved. On the 18th day, the patient completely recovered. Linezolid penetrates into the CSF and it has also good activity against both *E. faecium* and non-*E. faecium* species (*E. casseliflavus*) (3,8,14).

The present report stresses the need for clinicians to be aware of *E. casseliflavus* meningitis since the organism possesses an intrinsic low level vancomycin resistance and VanC phenotype. Proper management of infection by this rare organism warrants correct identification and sensitivity testing of such an isolate. Our attention should be drawn to serious infections caused by this motile organism even in patients without severe underlying disease or immunocompromised status. As a result, *E. casseliflavus* may cause rare central nervous system infections. The increasing resistance to treatment should be considered over time. A favourable outcome was observed with intravenous linezolid in this case report and it should be considered as a treatment option for similar cases. To our knowledge, our case is the first case in a pediatric patient and the third case of *E. casseliflavus* meningitis reported.

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