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CASE REPORT

Meningitis associated with Vancomycin resistant *Enterococcus casseliflavus*: First report

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ABSTRACT

Enterococci are present in the gastrointestinal system as normal floral components. In the past two decades members of the genus Enterococcus have emerged as important nosocomial pathogens worldwide. Enterococci may cause a range of different disorders such as urinary tract, intraabdominal, and wound infections, as well as endocarditis, meningitis and bacteraemia. Nosocomial enterococcal meningitis is most commonly observed following ventriculoperitoneal shunt operations. Vancomycin resistant enterococcus (VRE) represents 30% of all enterococci infections.

This report presents a vancomycin-resistant *Enterococcus casseliflavus* meningitis case in a 66-year-old patient with ventriculoperitoneal shunt, which has not been reported in the literature before. Successful outcomes were obtained with daptomycin plus linezolid combined treatment in VRE meningitis. Treatment recommendations in VRE meningitis are also discussed in this article. *J Microbiol Infect Dis 2011;1 (3):138-140*

Key words: Vancomycin-resistant enterococcus, *Enterococcus casseliflavus*, meningitis.

Vankomisine dirençli Enterococcus casseliflavus menenjiti: İlk olgu

ÖZET

Enterokoklar, gastrointestinal istemin normal flora elemanlarıdır. Enterokoklar geçen iki dekatta dünyada önemli nozokomiyal patojenler olarak karşımıza çıkmaktadır. Üriner sistem, intraabdominal, yara enfesiyonu, endokardit, menenjit ve bakteriyemi gibi farklı hastalıklara neden olabilir. Nozokomiyal enterokok menenjiti genellikle ventrikülöperitoneal şant operasyonlarını takiben gelişir. Vankomisine dirençli enterokoklar (VRE), tüm enterokok enfeksiyonlarının %30'unda etkendir.

Bu yazıda, ventrikülöperitoneal şantı olan 66 yaşında erkek hastada, daha önce literatürde bildirilmeyen Vankomisine dirençli *Enterococcus casseliflavus*' a bağlı menenjit olgusu anlatıldı. Daptomisin ve linezolidle tedavi edilen hasta iyileşti. Yazıda, VRE menenjitinde tedavi önerileri tartışıldı.

Anahtar kelimeler: Vankomisine dirençli enterokok, *Enterococcus casseliflavus*, menenjit.

INTRODUCTION

Enterococci are organisms that have developed well-adapted mechanisms to survive in the gastrointestinal tract of humans. Enterococci are clearly outnumbered by the amount of anaerobic commensals, and in a normal host, they appear to establish a symbiotic relationship with the immune system and the other bacteria.[1]

The commonest species are *E.faecalis* and *E.faecium*. Less commonly, *E.gallinarum* and *E.casseliflavus* may also be seen in nosocomial infections and immunosuppressed patients.[1,2] Vancomycin resistant enterococcus (VRE) represents 30% of all enterococci infections. More than 90% of VRE isolates are *E.faecium*.[2]

Enterococcal meningitis represents 0.3 to 4% of all cases of meningitis and has a high mortality. It may develop spontaneously or postoperatively. The typical presentation of enterococcal meningitis is rapid onset of fever, signs of meningeal irritation, and altered sensorium. Approximately half of spontaneous cases of meningitis are accompanied by bacteriemia.[3,4]

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This report presents a case of vancomycin resistant *E.casseliflavus* meningitis and bacteriemia, which have not been described in the literature before.

Clinical presentation and intervention

A 66- year old male patient was examined for high fever during hospitalization at the neurosurgery service. The patient underwent three revisional operations by the general surgery and neurosurgery services due to absorption problem at the point of entry of the ventriculoperitoneal shunt (VPS) to the peritoneum, which was placed one year ago for hydrocephalus, and due to sigmoid colon perforation. The shunt was replaced during the last operation.

On the hour postoperatively 12th hour, the patient had increased temperature (39.5°C), and a neck rigidity was revealed in the physical examination. Cerebrospinal fluid (CSF) analysis demonstrated 660 leukocyte/mm³. CSF protein was found as 200 mg/dl, CSF glucose as 4 mg/dl and simultaneous blood glucose values was found as 90 mg/dl. White blood cell was (WBC) 11,800/mm³, Hb 13.5 g/dl, platelet 427,000/mm³, CRP 18 mg/dl, and sedimentation 81 mm/h. The CSF, blood and urine samples were taken for culture and the treatment of nosocomial meningitis was started with vancomycin 2 g/day and meropenem 3 g/day.

The patient's fever continued during subsequent measurements, and the CSF and blood samples demonstrated *E.casseliflavus* growth after 48 hours. Bacteria identification was performed with the VITEK-2 system. Based on the Clinical and Laboratory Standards Institute (CLSI) criteria (MIC 2 mg/L via E test), the agent was vancomycin-resistant (MIC>32), daptomycin-susceptible (MIC 2 mg/L via E test) and linezolid susceptible (MIC 2 mg/L). Vancomycin treatment was discontinued and treatment with daptomycin 9 mg/kg/day was started. On the other hand, rectal swap culture of the patient showed vancomycin-resistant *E.casseliflavus* and *E.gallinorum* growth.

The patient had no neck rigidity after 48 hours of treatment. CSF sample was taken and analyzed which showed 50 leukocyte/mm³. There was no growth in the CSF culture. CSF culture on the 7th day of hospitalization also showed vancomycin-resistant *E.casseliflavus* growth. With no fever and neck rigidity and normal WBC count, the patient's CRP level improved. Patient's ventriculoperitoneal shunt was replaced. External CSF drainage was performed. Linezolid 600 mg/12 h was added to patient's treatment. There was no growth in blood or CSF sample. Patient's clinical status improved. Daptomycin-linezolid combined treatment was prescribed and he was discharged.

DISCUSSION

This report presents a vancomycin-resistant *E.casseliflavus* meningitis case which has not been reported in the literature before. Successful outcomes were obtained with daptomycin plus linezolid combined treatment in VRE meningitis.

Differing with age, vaccination status, comorbidities and geographical region, common causative factors of meningitis caused by Gram positive bacteria are *Streptococcus pneumoniae*, *Hemophilius influenzae* type b and *Neisseria meningitidis*. Lately, it is reported that Staphylococcus meningitis cases are increased; especially methicillin resistant *S.aureus* meningitis cases are more frequently encountered in postoperative patients.[1]

Enterococci are rare causes of meningitis. Enterococci are present in the gastrointestinal system as normal floral components. The cause in most of Enterococcus meningitis is *E.faecalis*. It has been reported that *E.faecalis* was observed in 90% of cases, followed by *E.faecium* and that *E.gallinorum* and *E.durans* may rarely be the cause.[5] Nosocomial enterococcal meningitis is most commonly observed following ventriculoperitoneal shunt operations. Shunt devices are a predisposing factor for nosocomial VRE.[6] Our patient was at risk for VRE meningitis associated with long-term hospitalization period and recurrent VPS operation.

The presented case differs from the literature in vancomycin resistance. CSF findings are usually similar to other bacterial meningitis. High protein and low glucose levels and neutrophil-dominant pleocytosis are seen, as was the case in our patient.

Several agents may be used in VRE meningitis, which include teicoplanin, chloramphenicol, rifampin, clindamycin, streptomycin, penicillin, amikacin given in different combinations. Today, there are several options in the treatment of VRE

infections such as quinupristin dalfopristin, linezolid and tigecycline.[1,7] There is, however, no specific recommendation for treatment of vancomycin-resistant enterococci meningitis. There are a limited number of cases in the literature and different combination treatments were administered to those patients.

Daptomycin was administered via the intraventricular route in two cases previously and successful outcomes were noted. The agent was administered to the infected shunt in one patient.[8,9] In a study with three cases of meningitis associated with vancomycin resistant *E.faecium*, combined daptomycin treatment was used for treatment of these patients. Two patients received daptomycin plus gentamicin and one received daptomycin and linezolid combination. Daptomycin was given at 9-12 mg/kg and gentamicin at 600 mg every 12 hours.[9]

In this study, sepsis was considered in the patient since there were bacteriemia and *E.casseliflavus* growth in blood cultures, and daptomycin treatment was efficient. On the other hand, reinfection from the peritoneum through the shunt was considered. Daptomycin is believed to be effective in VRE bacteriemia. Linezolid is a bacteriostatic agent which shows effect through inhibition of protein synthesis. 28-70% of it penetrates CSF.[10]

Successful outcomes were obtained with daptomycin plus linezolid combination treatment in shunt-mediated VRE meningitis. Improvements in clinical and CSF findings in a patient with ventriculoperitoneal shunt may be misleading for clinicians. Since microorganisms may form film layers over the shunt, antibiotherapy may not be effective particularly in patients infected with resistant microorganisms. Shunt removal must be planned at the start of treatment. Despite the limited number of cases in the literature, we believe that daptomycin and linezolid combination is a good choice for the treatment of VRE meningitis.

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