

## Early switch therapy from ceftriaxone to ampicillin in an immunocompromised patient with *Listeria monocytogenes* septicemia and meningitis

İmmün sistemi baskılanmış hastada *Listeria monocytogenes*'e bağlı sepsis ve menenjitin tedavisinde seftriaksondan ampisiline erken geçiş

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### ÖZET

*Listeria monocytogenes* is an important pathogen that may cause infection in the elderly and in immunocompromised patients with predisposing conditions. It can be an important cause of life-threatening bacteremia and meningoencephalitis in immunocompromised individuals. In this report, it was described a case of sepsis and meningitis caused by *L. monocytogenes* in a 39-year-old female with adenoid cystic carcinoma of the larynx. *L. monocytogenes* identification was performed at the species level using matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS, Bruker Daltonics, Germany). The patient was treated with an early switch therapy from ceftriaxone to ampicillin. This report indicates that early detection and treatment of *Listeria* sepsis and meningitis are important to obtain a better prognosis.

**Anahtar Kelimeler:** *Listeria monocytogenes*, meningitis, septicemia, MALDI TOF MS

### ABSTRACT

*Listeria monocytogenes*, yaşlılarda ve predispozan koşulları olan bağışıklık sistemi baskılanmış hastalarda enfeksiyona neden olabilecek önemli bir patojendir. Bu bakteri, bağışıklık sistemi baskılanmış kişilerde hayatı tehdit eden bakteriyemi ve meningoensefalitin önemli bir nedeni olabilir. Bu raporda, larenks adenoid kistik karsinomu olan 39 yaşındaki bir kadın hastada *L. monocytogenes*'in etken olduğu sepsis ve menenjit olgusu tanımlandı. *L. monocytogenes*'in tür düzeyinde tanımlanması matrix-assisted laser desorption and ionization time-of-flight mass spectrometry (MALDI-TOF MS, Bruker, Almanya) ile yapıldı. Hasta tedavide seftriaksondan ampisiline erken geçiş ile tedavi edildi. Bu rapor, *Listeria* sepsis ve menenjitinin erken saptanmasının ve tedavisinin, daha iyi bir prognoz elde edilmesindeki önemini işaret etmektedir.

**Key Words:** *Listeria monocytogenes*, menenjit, sepsis, MALDI TOF MS

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## INTRODUCTION

*Listeria monocytogenes* is a facultatively anaerobic non-spore-forming gram-positive bacterium. It is known to be responsible for severely invasive disease and it can cause sepsis, meningitis, and encephalitis (1). *L. monocytogenes* infection occurs predominantly in the following populations: elderly people, pregnant women, newborns, and immunodeficient patients; patients with chronic liver disease, malignant hemopathies, and diabetes; patients on chronic hemodialysis; and, less frequently, healthy individuals (2). The main route of transmission is confirmed to be through the consumption of contaminated food and via vertical transmission from mother to child (3). *L. monocytogenes* has the ability to cross three significant barriers in humans, such as the intestinal barrier, the blood-brain barrier and the fetoplacental barrier. It can invade normally nonphagocytic cells such as endothelial cells, enterocytes, and fibroblasts, utilizing certain surface invasion proteins, of which internalin A (InlA) and internalin B (InlB) are the best studied (4). Meningitis caused by this bacterium is associated with high mortality rates (5). Diagnosis of meningitis caused by *L. monocytogenes* is a challenge due to the absence of typical clinical symptoms (6). *L. monocytogenes* is considered susceptible to a wide range of antibiotics, such as ampicillin, tetracyclines, erythromycin, and gentamicin. However, most strains of *L. monocytogenes* exhibit intrinsic resistance to cefotaxime, cefepime, fosfomicin, oxacillin, and lincosamides (7). In this report, we describe a case of sepsis and meningitis caused by *L. monocytogenes* which developed after chemotherapy and radiotherapy for metastatic adenoid cystic carcinoma of the larynx. Patient was treated with an early switch therapy from ceftriaxone to ampicillin.

## CASE REPORT

A 39-year-old female with diffuse metastatic

adenoid cystic carcinoma presented to the Emergency Department of Hacettepe University Hospital because of fever and general weakness in June 2019. Patient was evaluated for infectious diseases because of high fever. Lumbar puncture (LP) was recommended as a preliminary diagnosis of central nervous system infection. Cranial magnetic resonance imaging (MRI) showed diffuse intracranial metastasis and edema. LP could not be performed due to widespread intracranial metastases. All diagnostic procedures and the treatment were performed after the informed consent had been obtained orally. Empiric acyclovir (3x10 mg/kg) and ceftriaxone (2x2 grams) were started. One set (one aerobic and one anaerobic bottles) of blood sample was taken for the culture. Bactec Plus Aerobic/F and Bactec Lytic (BD Diagnostic, USA) aerobic and anaerobic blood culture bottles were incubated in a Bactec FX instrument (BD Diagnostic, USA). Anaerobic blood culture bottle had a positive signal at the 19th hour of incubation. Microscopy of Gram-stained smears was performed for the positive blood culture bottle. Gram-positive rods were observed and clinicians were informed. Subcultures were performed in %5 sheep blood agar (BD, USA), schaedler agar (BD, USA), chocolate agar (BD, USA) and MacConkey agar (BD, USA), and incubated in aerobic (%5 sheep blood agar, chocolate agar and MacConkey agar) and anaerobic (schaedler agar) conditions. Semi-transparent colonies having beta-hemolysis were obtained from the aerobic culture at the end of 24 hours incubation, and Gram staining of the colonies showed gram-positive rods. The isolate was a catalase-positive, oxidase-negative, CAMP-positivite. Semi-solid motility test medium was used for detecting bacterial motility activity (BD, U.S.A) and the isolate was motile bacterium. Matrix-assisted laser desorption/ionization-time of flight mass spectrometry (Bruker, Germany) was used for the identification. The isolate was identified at the species level with a score of

$\geq 2.0$  as *L. monocytogenes*. Antibiotic susceptibility test was performed by gradient test according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines. Minimum inhibitory concentration of ampicillin, penicillin, meropenem, erythromycin, and trimethoprim/sulfamethoxazole were 0.38 µg/ml, 0.38 µg/ml, 0.19 µg/ml, 0.50 µg/ml, 0.032 µg/ml respectively. *L. monocytogenes* was susceptible to all tested antibiotics. Due to detection of *L. monocytogenes* from blood culture at the 48<sup>th</sup> hour of treatment, initial acyclovir and ceftriaxone therapy was changed to ampicillin (6x2 grams). Fever response was obtained at the 48th hour of the ampicillin treatment and CRP value decreased to 1.55 mg/dl. Control blood culture showed absolutely no growth. The patient was discharged after 21 days of ampicillin treatment with the diagnosis of Listeria bacteremia and a preliminary diagnosis of Listeria meningitis.

## DISCUSSION

An empirical therapy for bacterial meningitis, generally third-generation cephalosporins, is always applied at an early stage when bacterial meningitis is suspected. However, this treatment option does not cover *L. monocytogenes*. Cephalosporins, which are effective for some bacterial agents of meningitis, are ineffective against *L. monocytogenes*. This is important to remember in the empiric selection of drugs for pyogenic meningitis. Ampicillin is the preferred agent, resistance to this agent has not

been observed (8, 9). Listeria meningitis should be considered in cases that have immunosuppression and do not improve following first-line treatment with extended-spectrum cephalosporins. Unfortunately, adequate therapy might be delayed in our case, since initial empirical therapy was not adjusted to include ampicillin. Ampicillin should be added to initial empirical therapy especially for Listeria suspicion due to the risk factors. In this report, we described a case of meningitis and bacteremia caused by *L. monocytogenes* in a cancer patient. MALDI-TOF MS has become a standard tool for rapid and reliable microbial identification in clinical laboratories. Rapid and reliable identification of *L. monocytogenes* using MALDI-TOF MS allows a rapid detection of bacteria that cause a life-threatening infection and also provide accurate therapy. When *L. monocytogenes* was isolated from blood culture, antibiotic treatment was switched from ceftriaxone to ampicillin immediately, and the patient was cured. It is very important to adjust the appropriate antibiotic therapy as soon as possible once *Listeria* is highly suspected or confirmed by a culture. We encountered a case with sepsis and meningitis caused by *L. monocytogenes* which developed after chemotherapy and radiotherapy for metastatic adenoid cystic carcinoma of the larynx. Early management of sepsis and meningitis, by performing rapid diagnostic methods and by administration of adequate antimicrobial therapy, can be defined as life-saving circumstances in patients with listeriosis.

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