

A Rapidly Fatal Sepsis Caused by *Listeria Monocytogenes* Type-4b in A Patient with Chronic Renal Failure

Adem Kose¹; Yusuf Yakupogullari^{2,*}

¹Manavgat State Hospital, Infectious Diseases and Clinical Microbiology Clinic, Manavgat, Antalya, Turkey

²Medical Microbiology Department, Inonu University Medical Faculty, Malatya, Turkey

*Corresponding author: Yusuf Yakupogullari, Medical Microbiology Department, Inonu University, Medical Faculty, Malatya, Turkey. Tel: +90-5052782275, E-mail: yusufyakoup@yahoo.com

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Introduction: *Listeria monocytogenes* is a significant zoonosis causing invasive infections in the susceptible persons. The current paper presented a patient who died due to a rapidly-progressing multiple organ failure (MOF) as a result of severe sepsis caused by *L. monocytogenes*.

Case Presentation: A 70-years-old patient with chronic renal failure was admitted to the infectious diseases clinic due to diarrhea for one day. He was hospitalized and the body fluid samples were collected for laboratory analyses. Within few hours, his vital findings worsened, and he developed respiratory arrest. Ceftriaxone and gentamycin were administrated. However, he died due to disseminated intravascular coagulation, septic shock and meningoencephalitis at the 22nd hour of admission. Causative agent was identified as *L. monocytogenes* serotype-4b in post-mortem period.

Discussion: *L. monocytogenes* can cause progressive and rapidly fatal infections in the vulnerable persons, with multisystem involvement. Since this bacterium is not susceptible to cephalosporines, it will be better to consider effective antimicrobials in the treatment of the possible cases.

Keywords: *Listeria Monocytogenes*; Renal Failure; Sepsis

1. Introduction

Listeria monocytogenes is small, facultatively anaerobic, Gram-positive linear-motile rod. It is an intracellular pathogen causing zoonotic infections by consumption of contaminated milk and milk products, and processed meat. *Listeria* spp. can multiply in acid, bile and high-salt concentration environments as well as in high and low temperatures (1). *L. monocytogenes* causes two forms of listeriosis including the non-invasive listeriosis, a febrile gastroenteritis in immune-competent patients, and the invasive listeriosis that is frequently associated with septicaemia and/or meningoencephalitis in immune-compromised individuals. Furthermore, invasive listeriosis can manifest another form of clinical syndrome in pregnant women, and may cause abortion or birth of a stillborn of fetus with generalized infection (2). Additionally, *L. monocytogenes* is further reported as the causative agent of different types of invasive infections including brain abscess, rhombencephalitis, prosthetic joint infection, endocarditis and peritonitis (3). The current case presentation reported a patient with chronic renal failure, who developed septicaemia with multiple organ failure (MOF), and lost his life within 22 hours of hospitalization. The causative agent was identified as *L. monocytogenes* at post-mortem period. The authors further aimed

to emphasize the diagnostic and therapeutic challenges in *Listeria* spp. infections.

2. Case Presentation

A 70-years-old male patient was admitted to infectious diseases clinic with low-grade fever, abdominal pain and diarrhea for one day. In the first examination, his fever was 37.8°C, blood pressure 155/90 mm/Hg, and heart puls 100/min. His medical history included chronic renal failure for two-years with twice peritoneal dialysis in a week and hypertension for 13 years. He was hospitalized and body fluid specimens were collected for biochemical, hematologic and microbiological analyses. Hematologic findings included hemoglobin 10.3 g/dL, hematocrit %31.2, WBC count 16100/mL with %55 neutrophils and %45 lymphocytes. Biochemical values were as follows: sodium 128mEq/L, potassium 5.3 mEq/L, SGOT 805 u/L and SGPT 609 u/L. Stool and blood samples were collected for culture, and many neutrophils were observed in the stool microscopy. Presumptive diagnosis was considered as acute bacterial gastroenteritis and possibly salmonellosis or shigellosis.

Ceftriaxone 2 × 1g infusion was administrated empirically. However, his fever rose over 38.5°C, blood pressure

decreased and he lost his consciousness within some hours. Neck rigidity developed and he had convulsions. Low number of neutrophils and rare lymphocytes were observed in the cerebrospinal fluid (CSF). Minimal inflammatory changes were detected in the computerized tomography scan of the brain. The patient further developed abdominal rigidity and intestinal ileus. Neutrophils 600/mL was observed in the abdominal aspirate fluid sample. Serum levels of the liver enzymes, creatinine and urea augmented. Platelet count progressively decreased, and d-dimer and INR values increased. Fresh plasma was treated, and gentamycin 2 × 80 mg infusion was added to treatment. As he had respiratory arrest, he was mechanically ventilated. However, despite the intensive life support, the patient died due to cardiac arrest at the 22nd hour of his hospitalization. Two days later, automatized blood culture system (BD BacTec 9050, Becton Dickinson, USA) gave positive signal for this patient's sample.

Small, dirty-yellow bacterial colonies with narrow beta-hemolysis grew on the blood agar (Oxoid, UK). Gram-positive, non-spore-forming, catalase-positive, small bacillus was observed. It was motile in room temperature, hydrolyzed esculin, and did not produce hydrogen sulfide. The isolate was identified as *L. monocytogenes* in Vitek-II system (bio Mérieux, France). Antimicrobial susceptibility test showed that it was susceptible to penicillin, ampicillin, rifampin, ciprofloxacin, vancomycin, teicoplanin, imipenem, and gentamycin; but resistant to ceftriaxone, cefotaxime, and cefepime. Later, the isolate was classified in serogroup 4b with the application of Bacto-*Listeria*-O-antisera (Difco Lab, US).

3. Discussion

Despite the advances in diagnostic medicine and clinical microbiology, *L. monocytogenes*, a significant human pathogen, remains one of the least-recognized microorganisms. In spite of a potentially high risk of being exposed to this bacterium in everyday situations, the rate of infection and the chance of developing overt disease are rather low. This is possibly due to the fact that more contact will induce a transient colonization in the healthy individuals or, at most, a mild disease that is generally so non-characteristic that diagnostic tests are neglected (4). Therefore, many patients with noninvasive listeriosis remain unrecognized. However, if the patient has an immunocompromized situation, the course of infection is often severe and even fatal. Overall, approximately 20% to 30% of the patients with manifest invasive disease die (5). Therefore, prompt diagnosis and early administration of the appropriate treatment are critical to reduce mortality of the invasive infections caused by *L. monocytogenes*.

Listeriosis is an increasing concern worldwide. More than 50% growth in the incidence of listeriosis is noted from 2003 to 2006 in 25 European Union Countries (6). Similarly, Khatamzas et al. (7) reported that the prevalence of invasive listerial infection has increased about two-fold in the United Kingdom; however, the certain

reason(s) for these increases is still unexplained. Human listeriosis typically occurs as sporadic cases. However, nosocomial spread and also community epidemics are reported (3). In 2006, a large outbreak of listeriosis occurred in the Czech Republic, involved 78 patients of whom 13 died (8). Contaminated meat products and cheese were found as the source of the organism in majority of the epidemics and sporadic cases (3, 6, 7). In 2010, during a random inspection by the Agriculture and Food Ministry, 160'000 portions of hamburger meatballs of an international fast-food company were detected as contaminated with *L. monocytogenes*, in Turkey.

Almost 90% of the patients who develop invasive listeriosis are in a higher risk group. Healthy children and adults may also be infected with *L. monocytogenes*; however, they rarely become seriously ill. The following persons are particularly at high risk for the development of invasive diseases: pregnant women, the elderly, and the persons with weak immune system. Among these, the elderly constitute the largest group of victims for listeriosis. Centers for Disease Control and Prevention (CDC) report that 58% of the *Listeria* spp. infections occur in adults 65 and above. Furthermore, the persons in this group are almost four times more likely to get systemic listerial infections than the general population (9). On the other hand, approximately 10% of the patients have no known risk factor or underlying disease predisposing them to infection with *Listeria* (10). The current paper presented the case of an old patient with invasive listerial infection whose different body sites were involved.

The infection showed a rapid progression, and consequently, the patient lost his life within the first day of hospitalization. Possibly it was one of the shortest times of mortality caused by this infection. From a retrospective cohort study including 118 cases with listeriosis recorded within 23 years, Mitja et al. (11) reported that the factors predicting early mortality (death occurring 3-14 days after admission) were renal failure, previous corticosteroid treatment, and the age over 65. The present patient was compatible with these data. However, the mortality was observed in a shorter course of infection. Listeriosis frequently involves more than one organ or body system. Classical invasive disease manifests as a bloodstream infection. Meningitis is associated with 10% to 25% of the bacteremic patients (9). Rarely, uncommon involvement sites such as osteomyelitis, hepatitis, and endocarditis are reported (1, 3).

In the present case, the infection started with a gastrointestinal infection and progressed to a blood stream infection. Within 12 hours, symptoms of other organs involvement emerged, including neck rigidity and peritonitis. At the same time, positive findings for the infection were detected in both CSF (high pressure, many leucocytes, and low glucose) and in the peritoneal fluid (significant number of leucocytes and less number of Gram-positive bacillus). Subsequently, he developed disseminated intravascular coagulation. It was a further

unusual complication with systemic listeriosis. According to authors' knowledge, such complication was not reported previously. Finally, the patient died as a result of circulation shock and cardio-pulmonary arrest. No growth was achieved in the culture of the CSF and peritoneal fluid samples; on the other hand, *L. monocytogenes* was isolated from the blood culture samples. Unfortunately, the infecting organisms and their antimicrobial susceptibility pattern were defined after the patient's death. Then, the isolate was serologically grouped as *L. monocytogenes* 4b which was commonly reported from invasive infections and epidemics (12).

Despite the intensive efforts in the clinical microbiology laboratory, authors experienced diagnostic and therapeutic problems with the present case. In the first evaluation of the present patient, the most possible diagnosis was considered as salmonellosis. Therefore, ceftriaxone was commenced. However, after the pathogen was defined, it was realized that the initial therapy was not appropriate as a result of the natural resistance of *Listeria* spp. to later generation cephalosporines. Additionally, the infecting agent showed such a fast progression that the conventional culture methods failed to make a prompt diagnosis. Therefore, faster laboratory tests were required for timely diagnosis of such a rare but highly fatal infectious agent. From this point of view, serologic tests for *Listeria* spp. may be useful, since their results can be obtained earlier than those of the classical culture. However, these tests are sometimes impractical due to the frequent cross-reactions.

Nucleic acid amplification tests (NAATs) are another alternative for the early diagnosis of *Listeria*. Scott (13) reported that *L. monocytogenes* could be detected in the patients' blood samples within four hours, with a multiplex Polymerase Chain Reaction (PCR)-based assay. Therefore, these tests are considered promising for the rapid diagnosis of different types of pathogens including *Listeria* in a single reaction tube, within hours. On the other hand, the establishment of routine NAATs is not cost effective and feasible in every hospital. Hence, if NAATs are not available, serologic methods can be used with culture for early diagnosis of listeriosis. The current paper showed that listeriosis may progress to death of the patient within less than one day. Therefore, rapid laboratory tests are required for timely diagnosis of the

possible cases, and furthermore, it is better to consider appropriate antimicrobials when empirical treatment is planned for the patients suspected with listeriosis. After protection and food safety measurements, early diagnosis and early administration of effective treatment were found as the most important factors that can reduce the patient mortality.

Authors' Contributions

Dr. Adem Kose examined the patient, clinically followed, developed the original idea, collected data, wrote the manuscript, and was the guarantor. Dr. Yusuf Yakupogullari contributed to the development of the paper and data collection; he also performed some microbiologic analyses, and prepared the manuscript.

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