CASE REPORT / OLGU SUNUMU

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Listeria monocytogenes Bacteremia in Immunocompromised Patients: A Report of Two Cases

Listeria monocytogenes Bakteremisi: İki Olgunun Sunumu

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Abstract

Listeria monocytogenes is a Gram-positive, rod-shaped bacterium that can cause outbreaks through contaminated food. This report describes two cases of *L. monocytogenes* bacteremia successfully treated with a combination of meropenem and gentamicin. Both patients had underlying malignancies-multiple myeloma and breast cancer. Neither reported consuming unpasteurized milk or food from external sources. No relapse occurred in either case during a 6-month follow-up period. In conclusion, while *L. monocytogenes* bacteremia without associated meningitis or gastroenteritis is uncommon, it can occur in immunocompromised individuals. To our knowledge, these are the first reported cases of *L. monocytogenes* bacteremia in Bahrain.
Keywords: Glucose-6-phosphate dehydrogenase deficiency, central line-associated bloodstream infections, clabsi, transtuzumab, listeriosis

Öz

Listeria monocytogenes, kontamine gıdalar aracılığıyla salgınlara neden olabilen Gram-pozitif basillerdir. Bu yazıda meropenem ve gentamisin ile başarılı bir şekilde tedavi edilen iki *L. monocytogenes* bakteremi vakası sunuldu. Her iki vakanın da altta yatan maligniteleri vardı (multiple myeloma ve meme kanseri). Her iki olgu da pastörize edilmemiş süt ya da, dışarıdan gıda kullanımı yoktu. Her iki vakada da altı aylık takip süresince nüks olmadı. Sonuç olarak, menenjit veya gastroenterit ile ilişkili olmayan *L. monocytogenes* izole bakteremi vakaları çok yaygın olmasa da, immün yetmezliği olan bireylerde görülebilmektedir. Bildiğimiz kadarıyla, bu iki olgu Bahrain'den bildirilen ilk *L. monocytogenes* bakteremi vakalarıdır.
Anahtar Kelimeler: Glikoz-6-fosfat dehidrojenaz eksikliği, ateter ilişkili kan dolaşımı enfeksiyonu, kikde, transtuzumab, listeryoz

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Introduction

Listeria monocytogenes is a Gram-positive, rod-shaped bacterium that can cause outbreaks through contaminated food. It can lead to severe infections, including meningitis, bacteremia, and gastroenteritis, particularly in elderly and immunocompromised individuals[1-8]. This report describes two cases of *L. monocytogenes* bacteremia successfully treated with a combination of meropenem and gentamicin.

Case Report

Case 1

A 60-year-old Bahraini female was admitted to the Hematology-Oncology ward at Bahrain Oncology Centre with fever. She was referred to an Infectious Diseases consultant for antibiotics optimization. The patient had a diagnosis of Stage III multiple myeloma and a history of treated colon cancer (diagnosed in April 2016). She also had severe glucose-6-phosphate dehydrogenase deficiency. Her past medical history was otherwise unremarkable. Empirical treatment with piperacillin-tazobactam [4.5 g intravenous (IV) every 6 h] was initiated by the primary team while awaiting septic workup results. Blood cultures were obtained upon admission in the Emergency Department. Peripheral blood cultures (from both arms) grew *L. monocytogenes*, which was sensitive to meropenem but resistant to penicillin and cotrimoxazole. The patient did not have a central line. Following consultation with the Infectious Diseases team, piperacillin-tazobactam was discontinued after 6 days, and meropenem (1 g IV every 4 h) plus gentamicin (3 mg/kg IV once daily) were initiated. The patient exhibited no clinical signs of meningitis, presenting only with fever and flu-like symptoms. She denied consuming unpasteurized milk, food from external sources, or unregulated water. Blood cultures were repeated on the same day the antimicrobial regimen was modified and again 72 h later (two sets obtained 1 h apart). All follow-up blood cultures were negative. Inflammatory markers showed significant improvement, with C-reactive protein decreasing from 61 mg/l to 14 mg/l and procalcitonin from 25 ng/ml to 0.03 ng/ml. The patient remained afebrile after starting piperacillin-tazobactam. She completed a 14-day antibiotic course and was discharged in stable condition. There was no relapse during the 6-month follow-up.

Case 2

A 61-year-old Bahraini female was admitted to the Hematology-Oncology ward at Bahrain Oncology Centre due to poor oral intake and electrolyte imbalance (hypokalemia). She had metastatic breast cancer (with brain, liver, and bone involvement) and was receiving active treatment with monoclonal antibodies (trastuzumab emtansine). Her medical history also included diabetes mellitus, hypertension, and dyslipidemia. She had a central line (port-a-cath). She presented to the Emergency Department with poor oral intake and nausea. She denied consuming unpasteurized milk, food from external sources, or unregulated water. Routine urinalysis revealed white blood cell>100 and large leukocytes. C-reactive protein was elevated at 50 mg/l, and procalcitonin was 14 ng/ml. Empirical treatment with ceftriaxone (2 g IV every 24 h) was initiated, and a urine culture was sent. Twelve hours after admission, she developed hypotension (blood pressure 90/50), prompting a full septic workup and fluid resuscitation. Ceftriaxone was escalated to piperacillin-tazobactam (4.5 g IV every 8 h). Two days later, empirical vancomycin (1 g IV every 12 h) was added after preliminary blood culture results showed Gram-positive rods in both peripheral and port-a-cath samples. The Infectious Diseases team was consulted 3 days later following positive blood culture results. *L. monocytogenes* was isolated from both peripheral blood and port-a-cath cultures, with susceptibility to penicillin and meropenem but resistance to cotrimoxazole. The Infectious Diseases team recommended discontinuing piperacillin-tazobactam and vancomycin and initiating meropenem (1 g IV every 4 h) plus gentamicin (3 mg/kg IV once daily). They also advised port-a-cath removal and repeat blood cultures. A peripheral blood culture repeated 3 days after starting gentamicin and meropenem showed no growth. However, the port-a-cath sample grew *Pseudomonas luteola*, which was pan-sensitive. By that time, the port-a-cath had already been removed, and the patient was clinically improving, remained afebrile, and had decreasing inflammatory markers. C-reactive protein decreased from 50 mg/l to 28 mg/l, and procalcitonin dropped from 14 ng/ml to 0.28 ng/ml, with no leukocytosis. A subsequent peripheral blood culture grew methicillin-resistant *Staphylococcus epidermidis*, which later returned negative, and advised initiating linezolid IV only if the patient developed a fever. The port-a-cath had already been removed. During follow-up, the patient left the hospital against medical advice on day 11 of meropenem and gentamicin treatment. There was no relapse during the 6-month follow-up period.

Discussion

L. monocytogenes is a Gram-positive, non-spore-forming, motile, facultatively anaerobic, rod-shaped bacterium. It is catalase-positive and oxidase-negative and produces a beta-hemolysin that lyses red blood cells[1-3]. *L. monocytogenes* is naturally found in moist environments, including soil, water, and decaying vegetation and animals. It is challenging to eradicate from food processing facilities, as it can spread to food through contact with contaminated equipment or surfaces and continue

to grow in refrigerated conditions. However, it is easily destroyed by heating food to sufficiently high temperatures[1-3,8].

Human listeriosis is commonly transmitted through unpasteurized milk, soft cheese (due to their high moisture, low salt content, and low acidity), and raw meats such as cold cuts, hot dogs, and fermented or dry sausages. Additionally, cold-smoked fish, melons, and sprouts have been implicated in *Listeria* outbreaks[1-3,8]. *L. monocytogenes* can cause meningitis in neonates, the elderly, and immunocompromised individuals. In contrast, healthy individuals typically experience a self-limiting gastrointestinal illness with symptoms such as fever and diarrhea[5]. Among the elderly, *L. monocytogenes* is the third most common cause of bacterial meningitis, following *Streptococcus pneumoniae* and *Neisseria meningitidis*[9,10]. Cases of complications from bacteremia in central nervous system (CNS) listeriosis are relatively common, occurring in approximately 40% of cases, and are associated with a high mortality rate. Patients with *Listeria* infections affecting the CNS may present with symptoms such as altered mental status, fever, seizures, focal neurological deficits, and nuchal rigidity in about 60% of cases. According to the literature, the classic triad of fever, neck stiffness, and altered mental status is observed in 43% of cases, and nearly all patients exhibit at least two of the four hallmark symptoms: headache, fever, neck stiffness, and altered mental status[9,10]. Neither of our patients had an epidemiological link, nor did they exhibit signs of altered mental status or nuchal rigidity. Consequently, CNS listeriosis was deemed unlikely, and lumbar puncture was not performed due to the absence of classic meningitis symptoms. Both patients were immunocompromised and had no recent history of gastroenteritis. Nonetheless, they were treated as if they had CNS listeriosis[6]. Penicillin, ampicillin, and amoxicillin are the primary treatment options for *Listeria* infections. Combination therapy, such as adding gentamicin to ampicillin, has demonstrated the highest efficacy against the bacterium *in vitro*; however, gentamicin is ineffective against intracellular bacteria. Alternative treatment options include rifampin, vancomycin, linezolid, carbapenems, and quinolones, while trimethoprim is used in cases of beta-lactam intolerance[1-3,6,7]. Skogberg et al.[11] conducted a study on 74 patients with listeriosis, including immunocompromised individuals. In nine cases, cephalosporins-antibiotics with limited efficacy against *L. monocytogenes*-were administered. Among these, four patients died, including three with meningitis and one with bacteremia. In contrast, patients treated with antibiotics demonstrating strong in vitro activity against *L. monocytogenes*, such as penicillin G, ampicillin, or piperacillin-either alone or in combination with aminoglycosides-had better outcomes ($p<0.05$)[11]. In our study, both patients were treated with a combination of meropenem and gentamicin due to their underlying malignancies and immunocompromised status. As a result, both exhibited a significant and durable clinical response to this treatment regimen.

Conclusion

In summary, although isolated cases of *L. monocytogenes* bacteremia without associated meningitis or gastroenteritis are uncommon, they can occur in immunocompromised individuals. To the best of our knowledge, there are no previously reported cases of *L. monocytogenes* bacteremia in Bahrain.

Ethics

Informed Consent: Consent form was filled out by all participants.

Footnotes

Authorship Contributions

Concept: N.J., U.E., O.R.S., Design: N.J., U.E., O.R.S., Data Collection or Processing: N.J., U.E., A.K., N.B., A.R., S.H., O.R.S., Analysis or Interpretation: N.J., U.E., A.K., N.B., A.R., S.H., O.R.S., Literature Search: N.J., U.E., O.R.S., Writing: N.J., O.R.S.

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