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Case Report

Totally implantable venous access port infection with *Listeria monocytogenes*: 2 case reports at a tertiary center and literature review

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Abstract

Listeria monocytogenes infection in humans is mostly asymptomatic in immunocompetent patients. It rarely can cause self-limiting febrile gastroenteritis, bacteremia, meningoencephalitis, and maternal-neonatal infections. The latter three manifestations are the most common, especially among immunocompromised patients. We present two cases of *Listeria monocytogenes* bacteremia in cancer patients, a 79-year-old man and a 70-year-old woman in whom the source of bacteremia was identified to be the implantable venous access port (TIVAP). In both cases, the TIVAP has been removed after "positive control cultures the following readmission to the hospital despite targeted therapy with ampicillin and gentamicin". Removal of TIVAP was warranted to control the infection.

Introduction

Listeria monocytogenes is a non–spore-forming facultatively anaerobic Gram-positive rod-shaped bacteria. It can survive different extreme conditions such as wide pH range, high salt concentrations, and refrigeration temperatures [1]. *Listeria monocytogenes* can cause food-borne infections after consumption of unpasteurized milk products and undercooked food such as sausages, raw meat in particular turkey and chicken, and seafood (salmon, mussels) [1]. Although mostly asymptomatic in immunocompetent patients, infections with *L. monocytogenes* can cause self-limiting febrile gastroenteritis, or bacteremia, meningoencephalitis, and maternal-neonatal infections. The latter three manifestations are the most common, especially among immunocompromised patients. Infections with *L. monocytogenes* are more frequent in the two extremities of ages [1,2]. Implantable device-associated *L. monocytogenes* infections are described in the literature, but none of the described cases, except one, mentioned an implantable venous access port (TIVAP)-associated infection [3]. This article describes two cases of a TIVAP-associated infection with *L. monocytogenes.*

Case reports

Case 1

A 79-year-old man was admitted to the hospital on the 21st of September 2021 for a right colectomy due to relapsing colon cancer. The patient has been receiving chemotherapy since 2019, including Cetuximab and Capecitabine, through the TIVAP inserted on the 25th of September 2019. The last chemotherapy cycle was administrated one week before hospital admission. The Infectious Diseases Department was solicited to decide if post-operative antibiotic therapy was necessary. On history taking, the patient noted having multiple episodes of fever and chills at home before arriving at the hospital. However, no fever was documented at his admission. Blood tests done the day following the surgery showed a white blood cell count at 10500/mm [3], with 76.1% of neutrophils and a C-reactive protein (CRP) value of 136mg/L. CRP was not measured

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before surgery. Four blood cultures were then obtained at the same time, 2 from peripheral blood and 2 from the TIVAP. The patient has not been receiving any antibiotics. All blood cultures were positive for some Gram-positive rod-shaped bacteria. The differential time to positivity was 12h in favor of the set of blood cultures taken from the TIVAP. Subcultures on blood agar plates showed small, grey, translucent, drop-like, catalase-positive, b-hemolytic colonies, characteristic of the bacterial genus Listeria. The bacterial species *L. monocytogenes* was identified using a matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS). An antibiotic susceptibility testing, according to "Comité de l'antibiogramme de la Société Française de Microbiologie - European Committee on Antimicrobial Susceptibility Testing" (CA-SFM – EUCAST) [4] was performed. It revealed a susceptibility to ampicillin, meropenem, erythromycin, and the association of trimethoprim-sulfamethoxazole. This bloodstream infection was considered related to the TIVAP and antibiotic therapy with ampicillin 2g/4h IV was started. No adverse events were noted during the patient's hospital stay. The patient was then discharged on the 27th of September 2021 with amoxicillin 2g/4h per os and a daily dose of gentamicin 80 mg/12h IM. CRP level at discharge was 36mg/L and the white blood cells count at 6100/mm^3, with 60.8% of neutrophils.

Five days later, the patient was readmitted to the hospital for intestinal occlusion, resolved with conservative treatment. Blood tests taken on the readmission showed a white blood cell count at 6800/mm^3, with 59.4% of neutrophils and a CRP level of 15.9mg/L. Control blood cultures for the peripheral blood and from the TIVAP were then taken and the same antibiotics continued (ampicillin 2g IV/4h and gentamicin 80 mg IV/12h). Blood cultures from the TIVAP were positive again with *L. monocytogenes*, however, blood cultures from peripheral blood remained negative. Consequently, the TIVAP was removed and sent to the clinical microbiology laboratory for culture. The patient was then discharged. We should note that the outpatient stay between the two hospitalizations was uneventful. The culture of the TIVAP came negative.

Case 2

A 70-year-old woman with a history of pulmonary adenocarcinoma was treated with Keytruda through a TIVAP inserted on the 23rd of August 2012. The patient presented to the emergency department (ED) for left hemiparesis. Vital signs were normal, except for sinus tachycardia. Cerebral MRI (T1, T2, Flair, Diffusion with ADC and SWI sequences with gadolinium injection) was performed urgently and showed previously unknown cerebral lesions: one in the left occipital lobe (8 mm), one near the right caudate nucleus (6 mm) and two right frontal lesions (26 x 14 mm and 14 x 6 mm), with a hyper signal on FLAIR sequences. These lesions were considered cerebral metastases and radiotherapy sessions were started and the patient was then discharged.

Fifteen days later, the patient presented to the ED for increased weakness in the previously improving left side hemiparesis. A brain MRI was repeated, showing an increase in the size of the previously described lesions, with no new lesion identified. Ceftriaxone was initiated by the treating physician. No fever was detected. Four blood cultures were obtained at the same time, 2 from peripheral blood and 2 from the TIVAP. Two days later, the results of blood cultures obtained from the TIVAP showed the presence of *L. monocytogenes*. Antibiotic therapy was switched to gentamicin 5mg/kg/day IV for 5 days with ampicillin 2g/4h IV. In addition, perfusion was switched from TIVAP to peripheral access. The TIVAP was removed the following day and sent to the clinical microbiology laboratory for culture. A third cerebral MRI (sequences T1, T2, Flair, Diffusion with ADC and SWI, and after gadolinium injection) was then performed as well as an MR spectroscopy to differentiate between the neoplastic and infectious nature of the brain lesions. The result was in favor of brain abscesses. Antibiotic therapy was continued with ampicillin. A control cerebral CT scan was performed on day 18 of antibiotic therapy showing important regression of the brain lesions, which increases the probability of an infectious process rather than cerebral metastases. The antibiotic therapy was continued for a total of 45 days (35 days of in-patient treatment given intravenously and 10 days in the out-patient setting given per os). The culture of the TIVAP came negative.

Discussion

Patients with *L. monocytogenes* bacteremia had a mean age of 73 in the MONALISA trial with a standard deviation of 14. Our two patients had an age compatible with the literature results. The two patients described in our article had two identified major risk factors for *L. monocytogenes* bacteremia: older age and cancer [5].

Treatment of *L. monocytogenes* infections with aminopenicillin or benzylpenicillin alone or in combination with an aminoglycoside is considered the gold standard therapy. Acquired antimicrobial resistance in clinical practice is not commonly seen [6,7]. The argument behind the use of combination therapy is the fact that beta-lactams may have delayed bactericidal activity. Trimethoprim-sulfamethoxazole (TMP-SMZ) is considered an alternative option in case of beta-lactam allergy. The use of appropriate antibiotic therapy is associated with improved survival in patients with *L. monocytogenes* bacteremia, independently of any associated factor [5]. However, mortality of invasive *L. monocytogenes* infection remains high [5,6]. The optimal duration of therapy is three weeks due to the risk of relapse [7].

Implantable venous access port (TIVAP) infection with *L. monocytogenes* is rarely seen. To our knowledge, only one case report is described in literature [3]. Other implantable device-associated infections with *L. monocytogenes* are documented. A case report of an *L. monocytogenes* infection of a ventriculoperitoneal shunt in a child stated that the shunt was removed in 2 steps with cultures growing in both cases *L. monocytogenes* despite appropriate antibiotic therapy [8]. Other studies described cases of peritoneal dialysis catheter-related infections (peritonitis) with *L. monocytogenes* and endograft infections secondary to *L. monocytogenes* bacteremia [2,9].

Eleven case reports described aortic endograft infections caused by bacteremia of *L. monocytogenes.* The mean interval

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between graft insertion and infection was 25.55 months. All cases received guided antimicrobial therapy. Endografts were initially removed after diagnosis in three cases, in addition to guided antibiotic therapy. Delayed percutaneous drainage with surgical debridement was performed in one case whereas delayed percutaneous drainage alone was performed in another case. The remaining six cases did not undergo surgical interventions and were treated with guided antimicrobial therapy alone. Three of the six latter cases underwent surgical removal of the aneurysm and graft after recurrence in addition to the second course of guided antibiotic therapy. The mean interval between the diagnosis and the recurrence in these cases was 5.33 weeks [2].

In one study, 10% of bloodstream infections in patients with solid tumors were TIVAP-associated and 9% of bloodstream infections in the same population were caused by *L. monocytogenes* (but not related to a TIVAP) [10]. In another study of 742 oncology patients with solid tumors who had bacteremia, 20 patients (2.7%) had *L. monocytogenes* bacteremia, with a higher frequency in adults aged 75-year-old or more (4.6% for ≥ 75-year-old vs 1.9% for < 75-year-old; p-value 0.039), but bacteremia was infrequently related to catheter infections or endogenous sources in the older patients' group [11].

The decision to remove the TIVAP in the two cited cases was taken based on four factors. The first factor was the persistence of positive blood cultures taken from the TIVAP despite guided antimicrobial therapy and despite clinical improvement in the first case. The second factor was the fact that *L. monocytogenes* is known to form a biofilm in the food industry and attach to a variety of surfaces, including stainless steel, polypropylene, rubber polystyrene, and glass [12,13]. The third factor was the fact that, in patients with *L. monocytogenes* bacteremia, female sex (in the second case), older age, and ongoing neoplasia were identified as parameters associated with 3-month mortality in the MONALISA trial [5]. Finally, increased mortality was shown in patients with solid tumor and TIVAP infection when removal of the device was delayed [14].

Based on these data, and in order to reduce the risk of recurrence and mortality, the TIVAP was removed in the two cases. The absence of bacterial growth from the TIVAP culture could be related to technical limitations (absence of a sonicator at our hospital). We should note that in cases of suspected device-related bloodstream infection, blood cultures alone are sufficient to guide therapy [15].

For these reasons, studies should be conducted to find the optimal management to prevent *L. monocytogenes* bacteremia, especially in patients with ongoing malignancy who have TIVAP which constitutes a precious device in patients with the weakened vascular network, in addition to the financial burden which makes acquiring another port even more difficult.

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