



Case report

Listeria brain abscess in a patient with autoimmune hepatitis

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ABSTRACT

Listeria monocytogenes is an uncommon cause of brain abscesses. Immunocompromised hosts, pregnant women and patients at extremes of age are especially susceptible. We discuss the successful management of a woman with autoimmune hepatitis on prednisone and azathioprine therapy with a *L. monocytogenes* brain abscess. Previously thought to be a rare cause of central nervous system (CNS) infection, the incidence of CNS listeriosis has increased due to a rise in organ and bone marrow transplantation requiring immunosuppressive medications. *L. monocytogenes* brain abscesses are now more frequently described and are associated with high rates of concomitant bacteremia suggesting a hematogenous route of infection.

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Introduction

Listeria monocytogenes is a gram positive bacillus most commonly isolated in immunocompromised hosts, pregnant women and patients at extremes of age. It was first described as a new species in 1926, when isolated in laboratory rabbits [1]. In humans, it was first reported as a blood stream infection in a 17-year-old boy [2]. Subsequent reports have described both asymptomatic carriage, as well as invasive disease [2,3]. In this report, we discuss the successful management of a woman with autoimmune hepatitis on prednisone and azathioprine therapy who was found to have a *L. monocytogenes* brain abscess.

Case report

A 56-year-old woman presented to our institution with two days of acute onset right arm and leg weakness, which progressed to right hemiparesis. Her medical history was significant for autoimmune hepatitis diagnosed 3 months prior, for which she was prescribed prednisone 20 mg daily and azathioprine 100 mg daily. Prior to presentation, the patient had experienced chills, frontal headache and rhinorrhea. She denied fevers, night sweats, blurry vision, abdominal pain, nausea, emesis, diarrhea or rash. She

denied recent travel, consumption of unpasteurized cheese or changes in diet.

On presentation to the emergency room, vital signs were within normal limits. Physical exam was significant for decreased strength in the right upper and lower extremities, right patellar hyperreflexia and preserved sensation. The remainder of the exam was unremarkable. Her initial basic metabolic panel, complete blood count, erythrocyte sedimentation rate and C-reactive protein were all within normal limits. A computed tomography (CT) of the head without contrast revealed a left frontal mass with vasogenic edema. Magnetic resonance imaging (MRI) of the brain with and without contrast revealed two dominant left-sided peripherally enhancing brain lesions measuring 2.1 cm and 1.2 cm in size, with surrounding vasogenic edema and local mass effect.

On hospital day 3, she was febrile to 100.4 °F and her white blood cell count increased to 11.8 k/uL. Chest x-ray demonstrated no infiltrates. There was no evidence of urinary tract infection on urinalysis. She was started on empiric antimicrobial coverage with ceftriaxone, metronidazole and vancomycin for a suspected brain abscess. A lumbar puncture showed 48 cells/uL white blood cells with 89% neutrophils, 125 mg/dL protein and 63 mg/dL glucose. Her blood cultures grew gram positive rods (Fig. 1), rapidly identified via matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF) as *L. monocytogenes*, and her antimicrobial regimen was switched to ampicillin and gentamicin. Over the next two days, a total of three sets of blood cultures grew *L. monocytogenes*. On hospital day 5, she underwent an MRI-guided stereotactic aspiration of the left frontoparietal brain abscess with drainage of 2 mL of purulent material. The Gram stain was positive for gram positive rods and the bacterial culture

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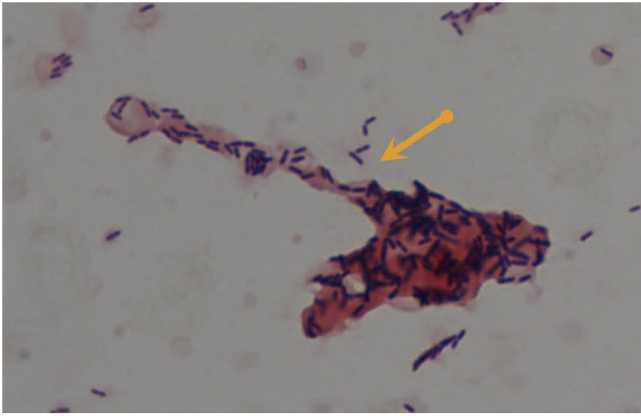


Fig. 1. Gram stain of blood culture showing gram positive rods (arrow).

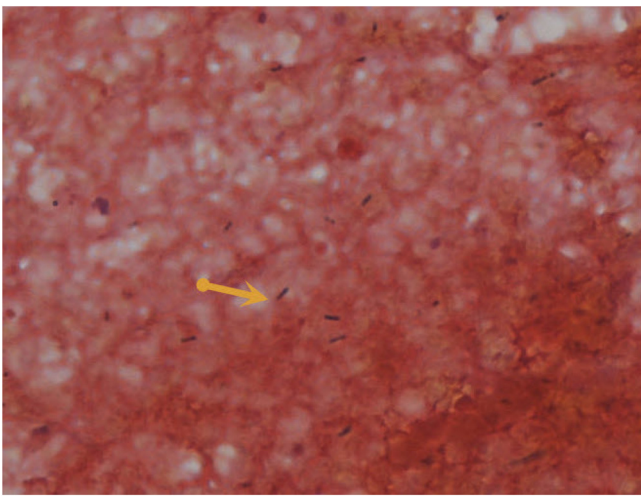


Fig. 2. Gram stain of brain abscess fluid showing gram positive rods (arrow).

also grew *L. monocytogenes* (Fig. 2). The patient clinically improved after drainage, and subsequent blood cultures were negative. She was discharged to an acute rehabilitation center with a plan to complete two weeks of gentamicin and six weeks of ampicillin. Four months later, she reported significant improvement in strength in her right upper and right lower extremities, however still required assistance with household activities.

Discussion

The genus *Listeria* consists of 7 species, including *L. monocytogenes*, *L. innocua*, *L. welshimeri*, *L. grayi*, *L. seeligeri*, *L. ivanovii* and *L. marthii*. *L. monocytogenes* is most commonly associated with human disease. It is a gram-positive bacillus that grows readily on blood agar, producing a narrow band of beta-hemolysis. It possesses peritrichous flagella, which give it characteristic tumbling motility, occurring only in a narrow temperature range, between 20 and 25 °C. *L. monocytogenes* is acquired via ingestion of contaminated food, and the majority of human infections occur in those with weakened cellular immunity. Once ingested, *L. monocytogenes* crosses the mucosal barrier and invades into the blood stream. Once phagocytosis within circulating leukocytes has occurred, the organism uses actin filaments to move to adjacent cells without being exposed to antibodies, thereby bypassing the humoral immune system and allowing for hematogenous dissemination. *L. monocytogenes* has a specific affinity for the central

nervous system, especially cell mediated immunodeficient individuals [4,5]. Infection of the central nervous system may occur via hematogenous spread, as a consequence of direct bacterial dissemination to and from the brain parenchyma or via retrograde axonal migration along the axons of cranial nerves [6]. In the past, lengthy culture-based techniques were used for identification of *Listeria*, requiring the organism to multiply at cooler temperatures. Recently, the use of MALDI-TOF MS has allowed for a more rapid and reliable identification of *Listeria* in patients with infection [7,8].

Previously thought to be a rare cause of central nervous system (CNS) infection, the reported incidence of CNS listeriosis has increased with the increased frequency of organ and bone marrow transplantation requiring the use of immunosuppressant medications. Since host defense against *L. monocytogenes* is predominantly cell-mediated, patients with physiologic or medication-induced defects in cell-mediated immunity, such as those on prednisone or azathioprine, are particularly vulnerable to infection. Corticosteroids such as prednisone are frequently used as immunosuppressive therapy, and can cause immunosuppression in a variety of ways, including the inhibition of phagocytosis and intracellular killing of pathogens [9]. Mice treated with corticosteroids and inoculated with *L. monocytogenes* showed prolonged fecal shedding of bacteria, as well as its persistence in the liver and spleen [10]. Azathioprine is an immunosuppressant agent that is FDA approved for renal transplant recipients and patients with rheumatoid arthritis. It is also used off-label for the treatment of autoimmune disorders, including autoimmune hepatitis. It is an antagonist of purine metabolism and functions by reducing intracellular purine synthesis, thereby suppressing cellular immunity and thus predisposing patients to infections [11]. Multiple experiments in mice have demonstrated that azathioprine prolonged the survival of *Listeria* inoculum and that those infected with a sublethal dose of *L. monocytogenes* while on azathioprine have a suppressed immune response, allowing for the growth of the organism in vivo [12,13].

Though still an uncommon presentation, *L. monocytogenes* brain abscesses have become more frequently described as well, with a high rate of concomitant bacteremia supporting the notion that the development is secondary to hematogenous spread [14]. Ampicillin has historically been the treatment of choice, with both in vivo and in vitro studies documenting a synergistic effect with the combination of an aminoglycoside, especially in cases of meningitis and endocarditis [15]. Intravenous trimethoprim-sulfamethoxazole has been used to successfully treat a 55 year old woman with an orthotopic liver transplant on azathioprine who was found to have *L. monocytogenes* bacteremia, and developed facial rash and urticaria while on oxacillin [16].

At our institution, we saw 9 cases of *L. monocytogenes* bacteremia in the previous 4 years. Though the number of yearly cases has remained steady, the use of MALDI-TOF allowed for earlier diagnosis when compared to previous methods. Our patient presented with symptoms concerning for a neoplasm, as she had no systemic signs of infection. She became febrile on the third day of hospitalization, and the blood cultures drawn at the time of fever allowed for rapid identification via MALDI-TOF. This represents a crucial step in the ultimate diagnosis of a *L. monocytogenes* brain abscess. Previously, *L. monocytogenes* brain abscesses have been described in immunosuppressed transplant patients, as well as a patient with autoimmune hepatitis on prednisolone [14,17]. Meningitis in a patient with autoimmune hepatitis on azathioprine has also been described, as well as cases in patients with autoimmune hepatitis who were post-transplant or on a medication other than azathioprine [18,19]. To our knowledge this is the first case of a *L. monocytogenes* brain abscess in a patient with autoimmune hepatitis on prednisone and azathioprine as the primary risk factors for infection.

Declarations of interest

None.

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References

- [1] Murray EGD, Webb RA, Swann MBR. A disease of rabbits characterised by a large mononuclear leucocytosis, caused by a hitherto undescribed bacillus *Bacterium monocytogenes* (n.sp.). *J Pathol Bacteriol* 1926;29(4):407–39.
- [2] Kaplan MM. Listerellosis. *N Engl J Med* 1945;232(26):755–9.
- [3] Nyfeldt A. Aetiology of Infective Mono-nucleosis. *Compte rendu des seances de la Societe de biologie* 1929;101:590–2.
- [4] Farber JM, Peterkin PI. *Listeria monocytogenes*, a food-borne pathogen. *Microbiol Rev* 1991;55(3):476–511.
- [5] Lorber B. Listeriosis. *Clin Infect Dis* 1997;24(1)1–9 quiz 10–1.
- [6] Disson O, Lecuit M. Targeting of the central nervous system by *Listeria monocytogenes*. *Virulence* 2012;3(2):213–21.
- [7] Barbuddhe SB, Maier T, Schwarz G, Kostrzewa M, Hof H, Domann E, et al. Rapid identification and typing of listeria species by matrix-assisted laser desorption ionization–time of flight mass spectrometry. *Appl Environ Microbiol* 2008;74(17):5402–7.
- [8] Jadhav S, Bhave M, Palombo EA. Methods used for the detection and subtyping of *Listeria monocytogenes*. *J Microbiol Methods* 2012;88(3):327–41.
- [9] Klein NC, Go CH, Cunha BA. Infections associated with steroid use. *Infect Dis Clin North Am* 2001;15(2)423–32 viii.
- [10] Prats N, Lopez S, Domingo M, Briones V, Garcia JA, Dominguez L, et al. Prolonged persistence of *Listeria monocytogenes* after intragastric infection in corticosteroid-treated mice. *Vet Microbiol* 1997;58(1):79–85.
- [11] Trotter JL, Rodey GE, Gebel HM. Azathioprine decreases suppressor T cells in patients with multiple sclerosis. *N Engl J Med* 1982;306(6):365–6.
- [12] Tripathy SP, Mackaness GB. The effect of cytotoxic agents on the primary immune response to *Listeria monocytogenes*. *J Exp Med* 1969;130(1):1–16.
- [13] Walencka M, Bloch M, Goscicka T. Effect of cyclosporine A (CsA), cyclophosphamide (Cy) and azathioprine (Aza) on the survival of *Listeria innocua* in mice. *Arch Immunol Ther Exp (Warsz)* 1994;42(4):275–9.
- [14] Eckburg PB, Montoya JG, Vosti KL. Brain abscess due to *Listeria monocytogenes*: five cases and a review of the literature. *Medicine (Baltimore)* 2001;80(4):223–35.
- [15] Mylonakis E, Hohmann EL, Calderwood SB. Central nervous system infection with *Listeria monocytogenes*. 33 years' experience at a general hospital and review of 776 episodes from the literature. *Medicine (Baltimore)* 1998;77(5):313–36.
- [16] Spitzer PG, Hammer SM, Karchmer AW. Treatment of *Listeria monocytogenes* infection with trimethoprim-sulfamethoxazole: case report and review of the literature. *Rev Infect Dis* 1986;8(3):427–30.
- [17] Limmahakhun S, Chayakulkeeree M. *Listeria monocytogenes* brain abscess: two cases and review of the literature. *Southeast Asian J Trop Med Public Health* 2013;44(3):468–78.
- [18] Tseng J, Strasfeld LM, Orloff SL. An unusual presentation of altered mental status after orthotopic liver transplantation: listeria brain abscess. *Transplantation* 2013;95(12):e72–3.
- [19] Gaini S. *Listeria monocytogenes* meningitis in an immunosuppressed patient with autoimmune hepatitis and IgG4 subclass deficiency. *Case Rep Infect Dis* 2015;2015:102451.