

# CASE REPORT

## *Listeria Monocytogenes* Meningitis in an Immunocompetent Adult

Peter Reardon<sup>1</sup>, Mark Reardon MD FRCPC<sup>2</sup>

<sup>1</sup>Class of 2014, Faculty of Medicine, Dalhousie University

<sup>2</sup>Department of Emergency Medicine, University of Ottawa

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### Abstract

*Listeria* is an uncommon cause of acute bacterial meningitis. It usually affects neonates, elderly, immunocompromised, and pregnant women with only a few cases among healthy, immunocompetent adults. Food exposure also represents an important risk factor for infection. Ampicillin administration is paramount to treatment as *Listeria* is intrinsically resistant to third-generation cephalosporins. However, *Listeria* meningitis is not easily diagnosed in the early stages. It is necessary to obtain an accurate history, and maintain a high index of suspicion in the appropriate setting. Early recognition of susceptibility, risk factors, and exposures can improve the outcomes of patients. Described is a case of *Listeria* meningitis in a previously healthy and immunocompetent adult who achieved a favourable outcome as a result of early recognition and proper treatment despite remaining undiagnosed at first presentation.

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### Case Presentation

A 60-year-old male presented to The Ottawa Hospital Emergency Department on June 24th, 2011 with headache, fever, and decreased level of consciousness. His past medical history was unremarkable, and he was not taking any medications. Six days prior to presentation, he had returned from a three-week trip to France, followed by a four-week cruise touring Italy, Spain, and some Adriatic states. Collateral history noted that he had ingested large quantities of soft cheeses in rural areas of these countries. He experienced a bout of diarrhea and suffered mild intermittent headaches over the course of the trip.

He had presented to a walk-in clinic the prior evening with fever and increasing headache. Routine bloodwork and malaria screen were negative. He was diagnosed with a viral illness and sent home. The following morning, his spouse found him increasingly drowsy and confused. She called 911 and he was brought to the emergency department by ambulance.

On examination the patient was obtunded, with a Glasgow Coma Scale (GCS) score of 11 (M5V2E4), and febrile with an oral temperature of 39.7 °C. No focal neurological signs were present. The cardiovascular, respiratory, and abdominal exams were unremarkable. Over a two-hour period the patient's GCS decreased to a level of 6. The patient was then intubated for airway protection and admitted to the intensive care unit.

The initial laboratory investigations returned the following results: WBC  $16.4 \times 10^9/L$  (neutrophils

$14.7 \times 10^9/L$ ), RBC  $4.48 \times 10^9/L$ , platelets  $193 \times 10^9/L$ , ESR 20 mm/hr, total bilirubin 27  $\mu\text{mol/L}$ , lactate 2.6 mmol/L. His serum electrolytes, blood glucose, and liver enzymes were all within normal limits. Chest X-ray showed increased interstitial markings and perihilar opacities. Computed tomography scan of the head was normal. A blood culture was performed and the patient was started on IV acyclovir, vancomycin, ceftriaxone, and ampicillin empirically. The first lumbar puncture performed was unsuccessful. A lumbar puncture performed the following day was successful. The patient's cerebrospinal fluid (CSF) was clear and colourless. It showed a marked pleocytosis (leukocyte count  $686 \times 10^6/L$ , neutrophils 0.41), RBC  $41 \times 10^6/L$ , protein level 1.33 g/L, glucose level 3.0 mmol/L. Gram stain of the CSF smear did not demonstrate any microorganisms. Magnetic resonance imaging (MRI) was not included in the work-up. His blood culture then grew *Listeria monocytogenes* in one aerobic bottle. Treatment was subsequently restricted to ampicillin only. Gentamicin was omitted as the patient had already been on ampicillin for two days and responding favourably to treatment. The patient was extubated two days later. He was neurologically intact and improved back to his pre-morbid condition. A peripherally inserted central catheter line was introduced and the patient kept on IV ampicillin for a total of three weeks.

### Literature Search

A search was conducted to examine the available literature concerning *L. monocytogenes* meningitis in immunocompetent adult populations. All types of

studies were considered. The MEDLINE database was searched with a 20-year restriction using the PubMed interface with the terms “listeria OR listeriosis” and “meningitis.” The search was limited to the English language and human studies, and yielded 336 results. Studies concerning paediatric populations, strictly immunocompromised patients, or nonspecific acute bacterial meningitis were excluded. The bibliographies of relevant articles were also examined for related papers. There is a paucity of literature pertaining to listeria meningitis in adult populations. The available studies consist of four observational studies, two case series, and four case reports. Details of these studies are included in Table 1.

### Discussion

Acute bacterial meningitis is a serious and potentially life-threatening illness. In Canada, incidence rates range from 3.37-3.66 per 100,000, with an overall case fatality rate of 11.3%.<sup>1</sup> In particular, *L. monocytogenes* is responsible for approximately 3-10% of bacterial meningitis cases<sup>1-4</sup> with case numbers being highest in pregnancy, neonates and the elderly (>60 years).<sup>5</sup> Travel to the European Union has also been associated with infection. The higher rates of Listeriosis in the European Union, which have significantly increased over the past five years,<sup>6,7</sup> are likely related to the types of food ingested by the population. However, the largest observational studies of listeria meningitis to date demonstrate that an immunocompromised state plays a role in up to 70% of cases, with relatively few cases being described among healthy, immunocompetent adults.<sup>8-10</sup>

*L. monocytogenes* infection is frequently contracted through consumption of contaminated food. Raw vegetables, unpasteurized dairy products, meat, and ready-to-eat foods are of particular concern as a result of their source and processing methods.<sup>5</sup> In Western European countries and some areas in Canada, it is common for restaurants and hotels to serve unpasteurized food products. Proper food hygiene can prevent contraction of Listeriosis and deadly sequelae such as meningitis and meningoencephalitis.<sup>5,11</sup>

The presentation of Listeria meningitis is variable. Symptoms can range from fever and headache, to cranial nerve palsies and seizures.<sup>8-10</sup> The rate of the classic triad presentation for bacterial meningitis (fever, neck stiffness, and altered mental status) is approximately 50%.<sup>8-10</sup> CSF findings are typical of acute bacterial meningitis with a pleocytosis, increased protein level and a decreased CSF/serum glucose ratio.<sup>8-10</sup> Amaya-Villar et al. performed a sub-group analysis to compare

the characteristics of community acquired Listeria meningitis with other bacterial etiologies. Preliminary data concerning the CSF profile of Listeria patients demonstrated significantly fewer leukocytes with a smaller percentage of polymorphonuclear cells, a lower protein count and less hypoglycorrhacia.<sup>8</sup> However, further multivariate analysis found only the CSF/serum glucose ratio to be independently associated with Listeria meningitis.<sup>8</sup>

The state of immunity may also influence the case presentation in Listeria meningitis. Immunocompetent patients more commonly present with brainstem encephalitis (rhombencephalitis).<sup>8,12</sup> As such, cerebellum dysfunction and various cranial nerve palsy deficits are more common in this group.<sup>8,12</sup> MRI is the most sensitive imaging modality in detecting changes related to Listeria rhombencephalitis with nearly 100% of patients having abnormal scans.<sup>12</sup> Although an MRI was not performed in the described case, treatment remains the same for both conditions.

Early and aggressive intravenous antibiotic therapy is the mainstay of treatment for bacterial meningitis. However, *L. monocytogenes* is intrinsically resistant to third-generation cephalosporins,<sup>13-15</sup> which is the empiric therapy for bacterial meningitis.<sup>15</sup> Resistance rates have been reported as high as 76% for ceftriaxone.<sup>13</sup> Ampicillin is an important adjunct, as it is first-line therapy for Listeria infection. In addition to having good penetration of the blood brain barrier, susceptibility studies have demonstrated low rates of resistance (less than 10%).<sup>13</sup> It is imperative that this antibiotic be added to the treatment regimen if there is any possibility of *L. monocytogenes* as the source of infection. Further studies of combination therapy have discovered a synergistic effect of aminoglycosides and ampicillin in listeriosis, with up to 100-fold increases in bactericidal activity.<sup>13-15</sup> The current standard treatment for Listeria meningitis is a combination treatment of ampicillin with gentamicin.<sup>13-15</sup> Aminoglycosides alone are not recommended due to poor central nervous system penetration and variable intracellular efficacy.<sup>14,17</sup> For patients allergic to  $\beta$ -lactam antibiotics, trimethoprim sulfamethoxazole has been recommended as the appropriate second-line agent.<sup>14</sup> Yet, the largest observational study of Listeria meningitis patients to date demonstrated an inadequate antibiotic treatment regimen in 30% of cases.<sup>9</sup> Delay in adequate treatment can lead to poor outcomes with a mortality rate of up to 28%.<sup>8</sup>

This case represents an unusual case of Listeria meningitis in an immunocompetent adult. Although

Table 1: *Listeria monocytogenes* meningitis in adult populations

Study	Description	Population	Outcomes / Findings
Amaya-Villar et al. 2011 <sup>8</sup>	Prospective observational study. 39-month period. 9 hospitals. Patients >14 years old admitted to hospital with community acquired bacterial meningitis	278 patients. 46 episodes of Lm meningitis	Immunocompromised 67%. Age, immunosuppression, CSF/blood glucose ratio independently associated with Lm meningitis. Classic triad 49%. Empirical therapy of IV ampicillin 79%. Mortality rate 28%
Brouwer et al. 2006 <sup>9</sup>	Prospective observational study. 3.5-year period. Patients >16 years with culture confirmed bacterial meningitis	696 patients. 30 episodes of Lm meningitis	All patients immunocompromised or >50 years old. Classic triad 43%. Coverage of initial antimicrobial therapy was microbiologically inadequate in 30% of cases. Mortality rate 17%, and 27% experienced an unfavorable outcome.
Chau et al. 2010 <sup>18</sup>	Case series	3 cases of Lm meningitis	Classic triad present in all 3 patients. All CSF culture positive. All blood culture negative. Mortality rate: 67%
Drnda et al. 2009 <sup>19</sup>	Case report	1 case of Lm meningoencephalitis	55-year-old male. Patient was immunocompetent. Classic triad presentation. CSF culture positive. Initial treatment did not include ampicillin.
Jamal et al. 2005 <sup>20</sup>	Case report	1 case of Lm meningitis	25-year-old male. Patient was immunocompetent with a nonsignificant past medical history. Febrile with meningismus, but oriented. Initial treatment did not include ampicillin.
Manfredi et al. 2006 <sup>21</sup>	Case report	1 case of Lm meningitis	Patient was immunocompetent. Achieved good outcome
Mylonakis et al. 1998 <sup>10</sup>	Retrospective observational study. 33-year period. Patients >16 years diagnosed Lm meningitis at a single hospital. Additional literature meta-analysis excluded as per paediatric inclusion	42 patients. 44 episodes of Lm meningitis	No predisposing risk factors/immunocompetence in 24%. Fever: 91%, meningeal signs 76%, altered mental status 74%, mortality rate 24%
Roed et al. 2012 <sup>22</sup>	Retrospective observational cohort study. 29-year period. Danish national study of patients >16 years diagnosed with Lm meningitis, and alive 1-year post diagnosis. Examined long term outcomes	183 patients total. 37.7% mortality in 1 year leaving 114 Lm meningitis patients. 1026 population controls	Patients >50 with double the 5-year risk of cancer diagnosis. Increased 5-year mortality rate in Lm meningitis patients (mainly death due to cancer). Patients >50 years with adjusted mortality rate ratio of 2.37 for the first 5 years post diagnosis, when compared to controls. After 5 years, the mortality is comparable
Zhang et al. 2012 <sup>23</sup>	Case report	1 case of Lm meningitis	34-year-old male. Patient was immunocompetent. Past medical history non-significant. Inadequate initial antibiotic therapy. Patient achieved good outcome
Zuniga et al. 1992 <sup>24</sup>	Case series	4 cases of Lm meningitis	All patients immunocompetent. Ages 39-75 years. All CSF culture positive. Only 1 blood culture positive. No mortality. No immunosuppressive conditions evolved in 2 year follow-up

Lm: *Listeria monocytogenes*, IV: intravenous, Classic triad: fever, neck stiffness, altered mental status

uncommon, this patient's history included features, which could have prompted the health care providers to consider *Listeria* as a potential source of infection. These include his age of 60 years, and his travel history to Europe where he had ingested large amounts of likely unpasteurized soft cheese. He was successfully treated and an optimal outcome was achieved as a result of a case-appropriate antibiotic regimen.

### Conclusion

*Listeria meningitis* is not easily diagnosed in the early stages as happened in this case. It is necessary to obtain an accurate history, and maintain a high index of suspicion in the appropriate setting. Early recognition of susceptibility, risk factors and exposures can improve the outcomes of patients.

#### Key Points:

- *Listeria meningitis* is a serious, uncommon illness with a mortality rate of up to 28%
- Major risk factors include age (both neonatal and >60 years), pregnancy, and immunocompromise
- Infection is usually through ingestion of contaminated foods such as unpasteurized dairy, contaminated raw vegetables or improperly prepared meat products
- Ampicillin should be added empirically to meningitis treatment where there is a possibility of *Listeria* infection as it is resistant to third-generation cephalosporins

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