SM Journal of Infectious Diseases

Case Report

Successful Treatment of Listeria Monocytogenes Meningitis Using Trimethoprim-Sulfamethoxazole (TMP/SMX) in an Immunocompetent Adolescent

Randal De Souza[1*], Laura Roberts[2], Kristin Sundy-Boyles[3], Willian Godoy[4] and Cristina Tomatis Souverbielle[1]

[1*]Department of Pediatrics, Division of Infectious Diseases, Nationwide Children's Hospital and The Ohio State University College of Medicine, Columbus, Ohio, United States

[2]Department of Pediatrics, Nationwide Children's Hospital and the Ohio State University College of Medicine, Columbus, Ohio, United States

[3]Department of Pediatrics, Division of Pediatric Hospital Medicine, University of North Carolina Children's Hospital, Chapel Hill, NC, United States

4Family Medicine - Grant Medical Center, Columbus, Ohio, United States

Abstract

Listeria monocytogenes is often associated with foodborne illness, with invasive infections reported at the extremes of age, but it can cause meningitis in immunocompetent hosts. We report a case of an adolescent male successfully treated with a second-line agent, with no residual sequelae.

Keywords: Listeria; Meningitis; Trimethoprim-sulfamethoxazole; Immunocompetent

Abbreviations: ED: Emergency Department; IV: Intravenous; CT: Computed Tomography; CRP: C-Reactive protein; ESR: Erythrocyte Sedimentation Rate; MRI: Magnetic Resonance Imaging; FLAIR: Fluid-Attenuated Inversion Recovery; LP: Lumbar Puncture; CSF: Cerebrospinal Fluid; PMN: Polymorphonuclear Leukocytes; TMP/SMX: Trimethoprim-Sulfamethoxazole; AKI: Acute Kidney Injury; ID: Infectious Diseases; NGAL: Neutrophil Gelatinase Associated Lipocalin

Introduction

Listeria monocytogenes is a facultative, gram-positive, intracellular, anaerobic organism found widely in environmental and animal reservoirs. Transmission occurs through consumption of unpasteurized dairy or contaminated animal-derived produce, or through occupational exposure [1]. Listeriosis is the third-most common foodborne illness in the United States (US), affecting approximately 1600 people per year and causing about 260 deaths. Recent outbreaks have been linked to pre-packaged vegetables, smoked meats and fish, soft cheeses, and ice cream due to the pathogen's ability to tolerate colder temperatures [2,3].

Listeriosis manifests as self-limited febrile gastrointestinal disease in immunocompetent hosts. The risk for invasive infection increases when cellular immunity is impaired. This includes patients at the extremes of age such as neonates or the elderly (age over 65 years), those with congenital or acquired immunodeficiency (including malignancy, human immunodeficiency virus, and transplant recipients), and pregnant individuals [1].

The classic presentation of Listeria monocytogenes meningitis, with fever, nuchal rigidity, and mental status changes is seen in less than half of elderly patients [4]. Infection in immunocompetent children and adolescents is rare, accounting for less than 5% of infections in the US [5].

We report a case of successfully treated Listeria meningitis in a healthy teenager who presented with uncommon management challenges.

Submitted: 23 January, 2024 | **Accepted:** 24 February, 2024 | **Published:** 27 February, 2024

***Corresponding author(s):** Randal De Souza, Department of Pediatrics, Division of Infectious Diseases, Nationwide Children's Hospital and The Ohio State University College of Medicine, Columbus, Ohio, United States

Citation: De Souza R, Roberts L, Sundy-Boyles K, Godoy W, Souverbielle CT, (2024) Successful Treatment of Listeria Monocytogenes Meningitis Using Trimethoprim-Sulfamethoxazole (TMP/SMX) in an Immunocompetent Adolescent. SM J Infect Dis 7: 3.

Case Presentation

A 16-year-old adolescent male was admitted to our hospital with five days of daily fevers, right upper quadrant abdominal pain, severe frontal headache, and intermittent body aches. He was transferred from an outside facility as his symptoms progressed to inability to tolerate oral intake due to vomiting and diarrhea, with altered mental status. He had been diagnosed with acute COVID-19 infection four days prior to presentation, with sick contacts in his family. Due to concerns for dehydration, he presented to the outside Emergency Department (ED) one day prior to admission, where he received three Intravenous (IV) normal saline fluid boluses and IV ceftriaxone (dose unknown) for treatment of a presumed infection with a peripheral leukocytosis of 19.3×10^9 cells/L, before being discharged home.

He presented again on day of admission to the outside ED for worsening abdominal pain and increasing confusion. Computed Tomography (CT) scan of the abdomen and pelvis revealed possible cholecystitis, so he was given a dose of IV clindamycin (600 mg) and transferred to our facility.

Initial labs were notable for hypernatremia to 130 mg/dL, elevated AST to 52 U/L, C-Reactive Protein (CRP) of 3.2 g/dL, and elevated Erythrocyte Sedimentation Rate (ESR) to 33 mm/hr. abdominal ultrasound revealed "increased uniform gallbladder wall thickness and scant pericholecystic fluid, as can be seen with cholecystitis".

Physical exam performed by the inpatient attending physician was significant for nuchal rigidity, positional nausea and vomiting, photophobia, severe headaches, altered mental status, agitation, and unusual facial movements. The ophthalmologic exam was notable for papilledema (1+ optic disc edema bilaterally).

A CT of the head was normal, but Magnetic Resonance Imaging (MRI) of the brain was compatible with findings of meningoencephalitis including mild Fluid-Attenuated Inversion Recovery (FLAIR) hyperintensities throughout the cerebral and cerebellar sulci, showing enhancement on post contrast images.

An emergent Lumbar Puncture (LP) was performed, with an opening pressure of > 55 mm H20. Cerebrospinal Fluid (CSF) analysis showed glucose of 34mg/dL and protein of 57 mg/dL, cell count of 827 cell/ mm^3 with 801 nucleated cells/mm^3 (70% Polymorph Nuclear Leukocytes (PMNs) and 21% lymphocytes). The BioFire® FilmArray® Meningitis/Encephalitis (ME) Panel was positive for Listeria monocytogenes, and subsequently, CSF culture demonstrated growth of the same organism, confirming the diagnosis.

The patient was empirically started on ceftriaxone (100 mg/kg per day), vancomycin (20 mg/kg every 6 hours), and acyclovir (10 mg/kg every 8 hours) following the LP. When results of the ME panel returned, he was transitioned to trimethoprim-sulfamethoxazole (TMP/SMX, 20 mg/kg/day divided every 6 hours) and gentamicin (7.5 mg/kg/day divided every 8 hours). This regimen was selected due to a history of a blistering rash and respiratory symptoms early in childhood with administration of amoxicillin, concerning for Stevens-Johnson syndrome-like reaction. The Allergy and Immunology team advised against antibiotic desensitization therapy in this critically ill patient.

The patient's severe headache and vomiting concerning for increased intracranial pressure required two more repeat LPs and initiation of acetazolamide. Repeat CSF culture was negative, allowing for gentamicin discontinuation after five days of therapy. He continued to have severe nausea and vomiting despite multiple anti-emetic agents and ultimately required total parenteral nutrition for malnutrition after failure of both nasogastric and nasoduodenal feeding due to tube dislodgement secondary to retching.

The patient also had Acute Kidney Injury (AKI) during his hospitalization. This persisted while on TMP/SMX (a potential pseudo-AKI), with a peak creatinine of 1.36 (mg/dL) that only mildly improved after discontinuation of gentamicin. This resolved by discharge after complete antibiotic discontinuation. He was treated for 19 days with IV antibiotics.

The Infectious Diseases (ID) team identified several epidemiologic risk factors. The patient lived in a rural area on a farm with multiple animals, which included dogs, cats, chinchillas, chickens, pigs, goats, sheep, horses, and cows. He frequently cared for several animals, including milking the cows and consuming home-grown produce. He worked at the local Mexican restaurant and although he denied consumption of unpasteurized dairy products, he frequently consumed meals at work. Several siblings had acute COVID-19 infection around the time of this infection.

As Listeria meningitis is an uncommon infection in an immunocompetent host, we completed a workup during hospitalization to screen for causes of innate and acquired immunodeficiency. Total immunoglobulin levels and lymphocyte counts were normal. Human immunodeficiency virus testing was negative. Genetic testing performed using the Invite Primary Immunodeficiency Panel revealed him to be a genetic carrier of the FINP1 gene, which in its autosomal recessive iteration is associated with recurrent infections, hypo-or agammaglobulinemia, and hypertrophic cardiomyopathy. Repeat brain MRI at discharge showed resolved inflammation and repeat eye exam had no evidence of papilledema.

Discussion

We present an unusual case of Listeria meningitis in an immunocompetent adolescent. Notable features include unusual age at presentation, absence of immunocompromised state, clinical improvement with a second-line antibiotic, and acute COVID-19 infection.

At the time of this case, there was an ongoing multistate listeriosis outbreak linked to ice cream.[3] However, our patient had not eaten the specific brand of ice cream nor traveled out of state. It is likely that the patient's initial gastrointestinal illness attributed to COVID-19 was listeriosis that escaped immune surveillance and established invasive infection. It remains unclear why this host experienced invasive infection, but it could be related to the concomitant viral infection.

There are no known randomized controlled trials for the drug (s) of choice or duration of therapy for listeriosis, but the widely accepted first-line antibiotic regimen for Listeria meningitis is ampicillin and gentamicin. Other antibiotics with activity against Listeria monocytogenes include TMP/SMX, fluoroquinolones, linezolid, or rifampin, but resistance to secondary agents reported in the literature increases the risk of treatment failure [6]. For penicillin-allergic patients, options include penicillin de-sensitization, or the use of secondary agents such as TMP/SMX or a fluoroquinolone, both of which have been used as alternative monotherapy in the setting of Listeria meningitis [7]. There are several case reports of successful treatment with TMP/SMX in the literature, with good outcomes [8].

We were fortunate enough to know the etiology of this patient's meningitis at an early stage, so systemic steroids were not indicated. Steroids have been shown to improve outcomes in tuberculous and Hemophilus influenzae meningitis but may worsen outcomes when used in Listeria meningitis [9].

The patient's AKI while on TMP/SMX required close Nephrology monitoring during his hospitalization. The literature has described cases of "pseudo-AKI" in patients on TMP/SMX and tenofovir, whereby decreased tubular excretion of creatinine causes spurious serum elevation [10]. Supportive evidence for this phenomenon in our patient includes other normal renal function markers including cystatin-C and Neutrophil Gelatinase-Associated Lipocalin (NGAL). This AKI resolved upon discontinuation of antibiotics, consistent with previous reports.

It is unclear if his nausea was related to TMP/SMX, acetazolamide, or both, but this started to improve after weaning acetazolamide. TMP/SMX was stopped the next day, ~1.5 days earlier than planned, due to complete resolution of MRI findings and concern that medications were prolonging his symptoms.

Due to his extended hospitalization, this previous athletic patient experienced severe deconditioning requiring assistance with ambulation and subsequently pursued outpatient physical therapy. He was seen at follow-up visits, where he was able to ambulate independently, returned to school, and was training for a marathon three months post-hospitalization.

Though Listeria meningitis is unusual in healthy adolescents,

suspicion must remain high in the setting of meningitis, cholecystitis, and the mentioned risk factors. The use of rapid multiplex CSF diagnostic panels was helpful in starting directed therapy promptly. This case adds to the literature of successful treatment with alternative regimens and underscores the importance of side effects that could mimic poor response to therapy or progression of disease. Maintaining a broad differential can help promptly identify an unusual presentation of this uncommon disease in an immunocompetent host.

References

1. Farley MM. Listeria monocytogenes. Principles and Practice of Pediatric Infectious Diseases. 2023; 797-802.
2. Listeria Outbreaks. Centers for Disease Control and Prevention (CDC). 2023.
3. Nutrition C for FS and A. Outbreak Investigation of Listeria monocytogenes: Ice Cream US. Food And Drug Administration. 2022.
4. Pagliano P, Ascione T, Boccia G, De Caro F, Esposito S. Listeria monocytogenes meningitis in the elderly: epidemiological, clinical and therapeutic findings. Infez Med. 2016; 24(2): 105-111. PMID: 27367319.
5. Thigpen MC, Whitney CG, Messonnier NE, Zell ER, Lynfield R, Hadler JL, et al. Bacterial meningitis in the United States, 1998-2007. N Engl J Med. 2011; 364(21): 2016-25. doi: 10.1056/NEJMoa1005384. PMID: 21612470.
6. Castellazzi ML, Marchisio P, Bosis S. Listeria monocytogenes meningitis in immunocompetent and healthy children: a case report and a review of the literature. Ital J Pediatr. 2018; 44(1): 152. doi: 10.1186/s13052-018-0595-5. PMID: 30594251; PMCID: PMC6311039.
7. Committee on Infectious Diseases AAoP, Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH. Listeria monocytogenes Infections (Listeriosis). Report of the Committee on Infectious Diseases. American Academy of Pediatrics. 2021.
8. Polat M, Kara SS, Tapısız A, Derinöz O, Çağlar K, Tezer H. Successful treatment of refractory listeria meningitis and bacteremia with trimethoprim-sulfamethoxazole in an immunocompetent child. Turk J Pediatr. 2016; 58(2): 220-222. doi: 10.24953/turkjped.2016.02.017. PMID: 27976567.
9. Tunkel AR, Hartman BJ, Kaplan SL, Kaufman BA, Roos KL, Scheld WM, Whitley RJ. Practice guidelines for the management of bacterial meningitis. Clin Infect Dis. 2004; 39(9): 1267-1284. doi: 10.1086/425368. Epub 2004 Oct 6. PMID: 15494903.
10. Fraser TN, Avellaneda AA, Graviss EA, Musher DM. Acute kidney injury associated with trimethoprim/sulfamethoxazole. J Antimicrob Chemother. 2012; 67(5): 1271-7. doi: 10.1093/jac/dks030. Epub 2012 Feb 20. PMID: 22351681.