Escherichia coli Meningitis in a 72-year-old Woman

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ABSTRACT

Spontaneous community-acquired meningitis caused by *E. coli* is rare in the adult population. It is associated with a high risk of morbidity and mortality. We describe a case of a 72-year-old woman who presented with altered mental status and neck stiffness and was found to have *E. coli* meningitis. Urine cultures grew *E. coli*, representing a likely source. The *E. coli* strain was identified as sequence type 73 (*E. coli* ST73). Her symptoms and laboratory values improved following antibiotic initiation, and she was discharged from the hospital to a rehabilitation facility.

KEYWORDS: *E. coli* ST73, gram-negative meningitis, bacterial meningitis, urinary tract infection

INTRODUCTION

Bacterial meningitis occurs in approximately 0.9 per 100,000 individuals per year in high-income countries and is associated with a considerable risk of neurological sequelae (ranging from 9.4% to 25%) and mortality (ranging from 6% to 54%).[1-4] In adults, bacterial causes most commonly include *Streptococcus pneumoniae* and *Neisseria meningitidis*, as well as *Listeria monocytogenes* in those greater than 50 years of age.[1] Gram-negative bacillary meningitis is estimated to represent only 6.1% of bacterial meningitis cases in adults, with *Escherichia coli* specifically only occurring in 1% to 3% of cases.[5–8] We present a case of spontaneous community-acquired *E. coli* meningitis in a 72-year-old woman on chronic steroids, highlighting the importance of considering *E. coli* as a cause of meningitis.

CASE REPORT

A 72-year-old woman presented with altered mental status for one day with a five-day history of generalized weakness and a mild headache. Past medical history included nephrolithiasis (most recent ureteral stent and lithotripsy one year ago) complicated by multiple urinary tract infections, chronic kidney disease, cardiomyopathy with an ejection fraction of 28%, atrial fibrillation, anemia of chronic disease, and gout treated with chronic steroids. She had no history of ear or sinus infection, neurosurgical intervention or epidural injections, or previous episodes of meningitis. She fell at home one week prior and was cleared from any acute injuries following medical evaluation and imaging. She denied any additional current symptoms, including no photophobia, dysuria, urinary frequency, fevers, or chills.

Vital signs revealed a blood pressure of 128/71 mmHg, heart rate of 59 beats/min, and temperature of 36.7°C. On physical examination, she was confused with a Glasgow Coma Scale (GCS) score of 14 (eyes 4, verbal 4, motor 6). She had neck rigidity with a positive Brudzinski's sign but no focal motor or sensory deficits. The remainder of the physical examination was normal.

Complete blood count and comprehensive metabolic panel were notable for a white blood cell (WBC) count of 11.7 × 10^9/L with an absolute neutrophil count of 11.2 × 10^9/L, hemoglobin of 8.3 g/dL, and creatinine of 1.4 mg/dL (baseline 1.1–1.3 mg/dL). Two sets of blood cultures were obtained. Urinalysis demonstrated 64 WBC/hpf, 3+ leukocyte esterase, and negative nitrates. Computed tomography (CT) of the brain did not show evidence of any acute intracranial abnormalities. Following imaging, the patient underwent lumbar puncture, revealing clear cerebrospinal fluid (CSF) with 180 nucleated cells/ccm, 94% polymorphonuclear neutrophils, protein level of 97 mg/dL (normal 15–60 mg/dL), and glucose of 30 mg/dL (normal 50–80 mg/dL). Gram stain of CSF fluid showed many polymorphonuclear leukocytes, and organisms were seen. CT abdomen and pelvis was obtained, showing a likely left renal subcapsular hematoma and nonobstructing bilateral nephrolithiasis. There was no evidence of deep infection or abscess.

Empiric intravenous acyclovir (550 mg q8h), ceftriaxone (2g q12h), and ampicillin (2g q6h) were started less than two hours after the lumbar puncture was performed. She was admitted to the hospital.

Over the next several days, she remained hemodynamically stable with no fevers and with improvement in her neck symptoms. CSF culture grew *E. coli* susceptible to ceftriaxone (and ampicillin, cefepime, gentamicin, meropenem). Acyclovir was discontinued on day two of her hospitalization. Her WBC normalized. Urine culture grew >100,000 CFU/mL *E. coli* and >100,000 CFU/mL *Klebsiella pneumoniae*, both susceptible to ceftriaxone. Blood cultures obtained prior to antibiotics showed no growth. Ceftriaxone was continued and ampicillin was discontinued. Magnetic

resonance imaging (MRI) of the brain and cervical spine did not show any intracranial or spinal abscess. She continued to recover without any complications and was discharged to a short-term rehabilitation facility on day six of her hospitalization. She was continued on IV ceftriaxone for a total of 21 days.

Whole genome sequencing was performed in-house using Illumina iSeq platform. Resistance genes and point mutations associated with drug resistance in *E. coli* were detected using ResFinder, while virulence genes and *E. coli* serotypes were detected using VirulenceFinder and SerotypeFinder respectively. The *E. coli* was identified as sequence type (ST) 73, serotype O2 H1. No antibiotic-resistant gene and/or mutation was detected. Multiple virulence genes were detected: Surface attachment (papA_F43, papA F9, papC, iha, yeh A,B,C, D), iron acquisition (*iucC*, *iutA*, *fyuA*, *ireA*, *iroN*, *sitA*, *irp2*), serum resistance (*iss*, *traT*), Uropathogenic specific protein (usp), toxin (astA, senB, cnf1, hlyA), microcin (mchB, mchC, mchF), and ion resistance (terC).

DISCUSSION

Pathogens causing bacterial meningitis in adults include *Streptococcus pneumoniae* (72% of all cases) and *Neisseria meningitidis* (11% of all cases) and in those greater than 50 years of age, *Listeria monocytogenes*.[2] There is usually little to no reference to other pathogens.[1] Although *E. coli* is a common cause of neonatal meningitis, it rarely causes meningitis in adults.[2,9] Among 667 cases of meningitis in Rhode Island between 1976 to 1985, only 10 cases (1.5%) were of community onset meningitis due to coliform bacteria in adults.[10] Several more recent cohort studies in Europe of community-acquired bacterial meningitis found only 1% to 3% were caused by *E. coli*.[5–8] Risk factors for community-acquired *E. coli* meningitis include chronic alcoholism, liver disease, diabetes mellitus, immunocompromise, immunosuppressive drugs, and cancer.[8,9] *E. coli* meningitis can occur following penetration of the blood-brain barrier secondary to head and spinal trauma, CSF leak, and neurosurgical intervention and associated complications, including ventriculoperitoneal shunts and gastrointestinal perforation.[11,12] We present a rare case of an older patient with chronic steroid use who developed spontaneous community-acquired *E. coli* meningitis secondary to a UTI with *E. coli*.

The classic triad suggestive of meningitis includes fever, neck stiffness, and an altered mental status.[2,13] This triad occurs only in 41% of patients with acute bacterial meningitis (fever in 74%, neck stiffness in 74%, and altered mental status in 71%), though occurs more frequently in patients over 60 years of age.[14] By comparison, the classic meningitis triad is reported in only 25% of patients with *E. coli* meningitis with a low incidence (41%) of fever at presentation.[8] Consistent with prior literature, our patient presented with altered mental status and neck stiffness, but she did not have a fever at presentation and she did not develop a fever at any point during her admission. This low incidence of fever in *E. coli* meningitis may be a reflection of the patient cohort at higher risk of developing *E. coli* meningitis, including older patients and those on immunosuppression,[8] such as our patient. Overall, our case again highlights that reliance on the meningitis triad could lead to a missed or delayed meningitis diagnosis, especially with *E. coli* as the causative organism.

Gram-negative bacillary meningitis occurs more frequently as a complication from bacteremia in the setting of a distant infection, with one study reporting a distant source of infection in 77.5% with gram-negative bacillary meningitis compared to only 34.6% in other causes of meningitis.[15] For *E. coli* meningitis, urinary tract infection has been identified as the most common portal of entry, occurring in 24-48%.[8,9,16] Additional sources may include pneumonia, septic arthritis, ear infection, primary bacteremia, and peritonitis.[8,9,16] *E. coli* bacteremia is quite common in these patients with positive blood cultures identified in 76–79%. Interestingly, our patient had a distant source of infection (i.e., UTI) but no evidence of bacteremia. Several cases of *E. coli* meningitis with a urinary source have been described, but blood cultures are either positive or not enough information is given to determine the presence or absence of bacteremia.[8,16–18] Our whole genome sequencing of the *E. coli* identified it as *E. coli* ST73, the predominant invasive strain reported to cause urinary tract infections and bacteremia.[19,20] *E. coli ST73* carries a significant amount of virulence genes and it is an exclusive human pathogen.[20] In a recent genomic study, *E. coli* ST73 was also reported to cause community-acquired meningitis in adults.[21] Unlike pediatric *E. coli* meningitis, there is no predominant *E. coli* strain to cause adult meningitis. *E. coli* meningitis portends a high risk of morbidity, including neurologic complications (52–53%), ICU admission (47%), and organ failure (45%), as well as a high risk of mortality (36–48%).[8,9,16] Death from *E. coli* meningitis may be related to the virulence of the strains.[16]

Empiric treatment of bacterial meningitis should be promptly initiated when meningitis is suspected. For patients older than 50 years of age, empiric antibiotics include ceftriaxone plus ampicillin (plus Vancomycin where prevalence of cephalosporin-resistant pneumococcus is greater than 1%).[2,19] Ceftriaxone is used for the empiric treatment of bacterial meningitis when a gram stain of the CSF does not show any bacteria, because it crosses the blood-brain barrier and has activity against penicillin-resistant *Streptococcus pneumoniae* as well as *Neisseria meningitidis*. It is also the most commonly used antibiotic for *E. coli* meningitis in the literature[9,20] and is expected to be active against most strains of *E. coli* in areas of low prevalence extended spectrum beta-lactamase (ESBL) or carbapenemase producing (CPO) *E. coli*.[8] Antimicrobial susceptibility testing showed that our patient's *E. coli* was susceptible to ceftriaxone.

In conclusion, spontaneous community-acquired *E. coli* meningitis is a rare entity in adults. Fortunately, ceftriaxone, an antibiotic used for the empiric treatment of bacterial meningitis when no organisms are seen on CSF gram stain, is active against most isolates of *E. coli*. As highlighted in this case, patients may not present with the classic meningitis triad and frequently have a distant source of infection, such as a urinary tract infection. *E. coli* meningitis in adults portends a high risk of morbidity and mortality.

References

1. Hasbun R. Update and advances in community acquired bacterial meningitis. *Curr Opin Infect Dis*. 2019;32(3):233-238. doi:10.1097/QCO.0000000000000543
2. Hasbun R. Progress and Challenges in Bacterial Meningitis: A Review. *JAMA*. 2022;328(21):2147-2154. doi:10.1001/jama.2022.20521
3. van de Beek D, Brouwer MC, Koedel U, Wall EC. Community-acquired bacterial meningitis. *Lancet*. 2021;398(10306):1171-1183. doi:10.1016/S0140-6736(21)00883-7
4. GBD 2016 Causes of Death Collaborators. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2017;390(10100):1151-1210. doi:10.1016/S0140-6736(17)32152-9
5. Domingo P, Pomar V, de Benito N, Coll P. The spectrum of acute bacterial meningitis in elderly patients. *BMC Infect Dis*. 2013;13:108. doi:10.1186/1471-2334-13-108
6. Bichon A, Aubry C, Dubourg G, et al. Escherichia coli spontaneous community-acquired meningitis in adults: A case report and literature review. *Int J Infect Dis*. 2018;67:70-74. doi:10.1016/j.ijid.2017.12.003
7. Aronson SM, DeBuono BA, Buechner JS. Acute bacterial meningitis in Rhode Island: a survey of the years 1976 to 1985. *R I Med J (1976)*. 1991;74(1):33-36.
8. Cabellos C, Verdaguer R, Olmo M, et al. Community-acquired bacterial meningitis in elderly patients: experience over 30 years. *Medicine (Baltimore)*. 2009;88(2):115-119. doi:10.1097/MD.0b013e31819d50ef
9. Dzupova O, Rozsypal H, Prochazka B, Benes J. Acute bacterial meningitis in adults: predictors of outcome. *Scand J Infect Dis*. 2009;41(5):348-354. doi:10.1080/00365540902849391
10. Bodilsen J, Brouwer MC, Kjærgaard N, et al. Community-acquired meningitis in adults caused by Escherichia coli in Denmark and The Netherlands. *J Infect*. 2018;77(1):25-29. doi:10.1016/j.jinf.2018.05.009
11. Durand ML, Calderwood SB, Weber DJ, et al. Acute Bacterial Meningitis in Adults – A Review of 493 Episodes. *New England Journal of Medicine*. 1993;328(1):21-28. doi:10.1056/NEJM199301073280104
12. Bijlsma MW, Brouwer MC, Kasanmoentalib ES, et al. Community-acquired bacterial meningitis in adults in the Netherlands, 2006-14: a prospective cohort study. *Lancet Infect Dis*. 2016;16(3):339-347. doi:10.1016/S1473-3099(15)00430-2
13. Pomar V, Benito N, López-Contreras J, Coll P, Gurguí M, Domingo P. Spontaneous gram-negative bacillary meningitis in adult patients: characteristics and outcome. *BMC Infect Dis*. 2013;13:451. doi:10.1186/1471-2334-13-451
14. Moussiegt A, Birgy A, Cointe A, Duval X, Bidet P, Bonacorsi S. Escherichia coli community-acquired meningitis in adults: a case series of 29 patients in France. *Clin Microbiol Infect*. 2022;28(9):1304-1305. doi:10.1016/j.cmi.2022.04.020
15. Gilmore RL, Lebow R, Berk SL. Spontaneous Escherichia coli K1 meningitis in an adult. *South Med J*. 1983;76(9):1202-1203. doi:10.1097/00007611-198309000-00044
16. Ishida K, Noborio M, Nakamura M, Ieki Y, Sogabe T, Sadamitsu D. Spontaneous Escherichia coli bacterial meningitis mimicking heatstroke in an adult. *Clin Case Rep*. 2016;4(4):323-326. doi:10.1002/ccr3.509
17. Tunkel AR, Hartman BJ, Kaplan SL, et al. Practice guidelines for the management of bacterial meningitis. *Clin Infect Dis*. 2004;39(9):1267-1284. doi:10.1086/425368
18. Bouadma L, Schortgen F, Thomas R, et al. Adults with spontaneous aerobic Gram-negative bacillary meningitis admitted to the intensive care unit. *Clin Microbiol Infect*. 2006;12(3):287-290. doi:10.1111/j.1469-0691.2005.01346.x
19. Riley LW. Pandemic lineages of extraintestinal pathogenic Escherichia coli. Clin Microbiol Infect. 2014 May; 20(5):380–90. [PubMed: 24766445]
20. de Souza da-Silva AP, de Sousa VS, Martins N, da Silva Dias RC, Bonelli RR, Riley LW, Moreira BM. Escherichia coli sequence type 73 as a cause of community acquired urinary tract infection in men and women in Rio de Janeiro, Brazil. Diagn Microbiol Infect Dis. 2017 May;88(1):69-74. doi: 10.1016/j.diagmicrobio.2017.01.024. Epub 2017 Feb 7. PMID: 28214224; PMCID: PMC5392417.
21. Moussiegt A, Birgy A, Cointe A, Duval X, Bidet P, Bonacorsi S. Escherichia coli community-acquired meningitis in adults: a case series of 29 patients in France. Clin Microbiol Infect. 2022 Sep;28(9):1304-1305. doi: 10.1016/j.cmi.2022.04.020. Epub 2022 May 12. PMID: 35568305.

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Disclosures

No potential conflict of interest was reported by the authors.

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