IDCases 29 (2022) e01550

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcases

Case report

Bacteroides meningitis in a healthy child: A case report and review of the literature

Mamta D. Shah, Bruce K. Chy, Nathan B. Price *

University of Arizona College of Medicine, Banner University Medical Center, Tucson, USA

ARTICLE INFO

Keywords:
Anaerobic meningitis
Bacteroides
Molecular diagnostic testing
16s rRNA

ABSTRACT

A 7-year-old male presented with meningitis. CSF gram stain showed gram negative rods, but the organism failed to grow on culture. 16 s rRNA sequencing identified the organism as *Bacteroides fragilis*. The patient fully recovered with antibiotic therapy targeting that organism.

Introduction

In the vaccine era, the occurrence of bacterial meningitis in a previously healthy child is a rare event. Despite this the occasional infection with typical bacteria such as *Streptococcus pneumoniae* and *Neisseria meningitidis* can occur. Meningitis due to anaerobic bacteria is an exceedingly rare event and can be difficult to diagnose. We describe a case of meningitis in a previously healthy child caused by *Bacteroides fragilis* diagnosed by 16s rRNA sequencing.

Case

A 7-year-old male with no significant past medical history was transferred to our facility for evaluation after a history of fever, headache, and seizure. The fevers started 6 days prior to transfer. Within 48 h of fever onset, patient began to have headaches and abdominal pain, but denied photophobia, neck stiffness, nausea, or vomiting. Four days prior to presentation, patient was seen by a physician in Mexico who prescribed a course of trimethoprim-sulfamethoxazole for possible pharyngitis. Despite antibiotic treatment, symptoms persisted, and patient was taken to an outside ED in Southern Arizona one day prior to presentation. At the outside ED, the patient received a one-time dose of benzathine penicillin prior to being discharged home. At home his fevers worsened, and he had a tonic seizure. He was then immediately re-evaluated in the local ED at which time he was somnolent. Labs showed normal complete blood count with differential and complete metabolic panel (CMP). He was then transferred to our facility.

Upon arrival he was tachycardic and febrile to 38.5 C. He was irritable, restless and did not respond to commands though did open his eyes intermittently without making eye contact or communicating with others. The rest of his exam including neck, pharynx and abdomen were all normal. CMP was normal except for sodium of 129 mmol/l, potassium of 3.4 mmol/l and CO_2 of 19 mmol/l. Peripheral glucose was 145 mg/dl. The patient was sedated, and CSF was obtained by lumbar puncture. CSF showed 1350 white blood cells (73% neutrophils, 11% lymphocytes, 17% monocytes), 11 red blood cells, glucose of 72 mg/dl and protein of 79 mg/dl. Spinal fluid gram stain showed white blood cells and gram-negative rods (GNR). He was given hypertonic saline for hyponatremia and started on empiric vancomycin, ceftriaxone, and acyclovir.

Within several hours of the lumbar puncture and initiation of antibiotics he returned to baseline mental status and his fevers and headaches resolved. Given his history of pharyngitis metronidazole was added to cover anaerobic organisms such as *Fusobacterium spp*. Maxillofacial CT showed bilateral tonsillar lymphoid prominence but was otherwise normal. Brain MRI was normal. Blood culture, CSF HSV and enterovirus PCR, nasopharyngeal swab PCR for SARS-CoV-2, urinalysis and urine toxicology screen were all negative. CSF culture did not grow any organism and fluid was sent for 16 s rRNA sequencing. He did not have any additional problems and completed an empiric 10-day course of IV ceftriaxone, vancomycin and po metronidazole and was discharged. At that time, he did not have any abnormal symptoms or exam findings. The day after discharge, the 16 s rRNA sequencing resulted, detecting *Bacteroides fragilis*. He was given another 7 days of po metronidazole out of an abundance of caution. At follow up in clinic 3 weeks after completing his antibiotic course he had no abnormal symptoms

* Correspondence to: 1625 N Campbell Ave, Tucson, AZ 85719, USA.
E-mail address: pricen@peds.arizona.edu (N.B. Price).

https://doi.org/10.1016/j.idcr.2022.e01550
Received 8 April 2022; Received in revised form 20 June 2022; Accepted 22 June 2022
Available online 24 June 2022

and had a normal physical exam.

Discussion

The case detailed above presents a unique scenario of meningitis secondary to Bacteroides fragilis, a gram-negative anaerobic organism. Common microbes associated with bacterial meningitis in children beyond the neonatal period include *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type b (Hib).1 Anaerobic organisms, however, remain an uncommon source of bacterial meningitis. The challenges with identifying anaerobes via standard CSF cultures further limits our knowledge regarding the true incidence of anaerobic meningitis. Current literature regarding management of bacterial meningitis secondary to anaerobic organisms is largely limited to case reports.2.

CNS infections secondary to anaerobic organisms are typically polymicrobial and associated with spread from local infections of the sinuses, middle ear, oropharynx. Common microbes include *Bacteroides fragilis*, *Fusobacterium necrophorum*, Peptostreptococcus and *Clostridium sporogenes*.2 Patients with ventriculoperitoneal (VP) shunts are particularly susceptible to *B. fragilis* infection in the setting of intestinal perforation.1 The patient presented in the case above had a recent history of oropharyngeal infection treated by an outside physician thereby increasing the suspicion for an anaerobic etiology of meningitis.

Anaerobic meningitis is difficult to differentiate from aerobic meningitis based on clinical presentation as both will present with neurologic symptoms including but not limited to altered mental status, seizures, headaches, photophobia, etc.3 However, there exist risk factors that should increase clinical suspicion for anaerobic meningitis.

Amongst the neonatal population Group B streptococcus and gram-negative enteric organisms remain the most common etiologies of meningitis [1]. However, anaerobic meningitis has been reported amongst neonates, particularly in the setting of prematurity, maternal infection and premature rupture of membranes as detailed by Silvia, et al. [3] and Ziebold [4]. Of particular importance, initial cultures in both cases were negative. Silva, et al. isolated *B. Fragilis* after obtaining a culture from purulent contents drained from an empyema that developed.3 Ziebold obtained 3 LP samples prior to development of a positive culture.4 These two cases highlight the importance of considering anaerobic meningitis as an etiology of infection in the setting of negative cultures and worsening of symptoms despite empiric antibiotic therapy.

Additional risk factors for development of anaerobic meningitis in the neonatal period include congenital malformations, gastrointestinal perforation, and necrotizing enterocolitis.5 Aucher et al. detail a case in which *B. fragilis* meningitis was noted in a 2.5 month old infant who was underwent a rectoscopy in the setting of bloody diarrhea 2 days prior to presentation with neurologic symptoms [5]. Brook et al. presented a 5 month old male who developed a *B. fragilis* meningitis due to infection of a pilonidal sinus tract [6]. Cooke discussed the development of *B. fragilis* meningitis in a 16 day old term infant who was found to have an inguinal hernia with intestinal perforations at the level of the constriction causing fecal peritonitis [7]. And Feder discusses a case in which a premature neonate (32 weeks) developed *B. Fragilis* meningitis in the setting of necrotizing enterocolitis and subsequent perforation [8]. These cases demonstrate how intraabdominal pathology in the neonatal period poses a serious risk for the development of anerobic meningitis. Clinicians should therefore consider addition of empiric therapy for anaerobic organisms in patients with known intrabdominal pathology who develop neurologic symptoms.

Beyond the neonatal period, the primary risk factor for development of anaerobic meningitis is a history of mastoiditis, otitis media, or nasopharyngeal infection. [2] The development of anaerobic meningitis in pediatric patients with recent ear, nose, and sinus infections has been described by Kalay et al. [2], Martinez et al. [9], and Odugbemi et al. [10]. Therefore, as with our patient, maintaining a high index of suspicion for anaerobic meningitis in the setting of a recent oropharyngeal or sinus infections is critical for pediatric patients who fail to improve with empiric antibiotic therapy.

Identification of anaerobic organisms in the diagnosis of meningitis is challenging as these organisms are difficult to culture and differentiate from normal flora [11]. Particular methods with regards to specimen collection, transport and processing are required for appropriate identification of anaerobic organisms [1]. Despite meticulous collection and processing methods, identification of the organism may take up to 72 h and it is not uncommon for specimens to yield no growth despite positive gram staining particularly in the setting of recent antibiotic exposure as in our case [11]. The time-consuming and occasionally non-definitive process can delay clinical care and treatment with appropriate antibiotic therapy [12]. These challenges have resulted in the development of alternative methods for identifying anaerobic organisms. Recent advances include 16S rRNA gene–based methods, DNA hybridization, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), polymerase chain reaction, and oligonucleotide array technologies [11]. In our case, the inability to identify an organism via culture prompted further testing via the 16 S rRNA gene sequencing method and allowed for the identification of *B. fragilis* as a causative organism. Going forward, widespread use of molecular methods may allow us to better understand bacterial gene sequences and identify genes associated with antibiotic resistance [12].

Appropriate management of anaerobic infections often requires preventing further dissemination of the organism by achieving local control via drainage or debridement when indicated [1]. Antimicrobial therapy requires coverage of anaerobic organisms. Antibiotic therapy targeted at Bacteroides may include metronidazole, beta-lactam plus beta-lactamase inhibitors, carbapenems, and chloramphenicol. Resistance against penicillin and clindamycin is notable and therefore not recommended for management of infections caused by Bacteroides species. [13] In the current literature, metronidazole has been the agent of choice in treatment of Bacteroides meningitis due to its bactericidal effects and good CNS penetration. Treatment for 14 days is common; however longer duration of treatment up to 8 weeks has been noted in more complicated cases. [14] Commonly associated complications include brain abscesses, subdural or epidural empyema, ventriculitis and VP shunt placement for management of hydrocephalus [2]. Despite adequate treatment, only 30% of patients experience full recovery with the remainder experiencing neurologic sequelae [14]. Mortality has been noted to be as high as 34% [2].

The poor prognosis associated with unrecognized Bacteroides meningitis requires clinicians to maintain a high index of suspicion in pediatric patients, particularly those with recent oropharyngeal or otitis infections. This case also demonstrates the significance of innovative molecular technologies that improve identification of organisms. Finally, early treatment with appropriate antibiotic therapy is critical for long-term outcomes. In this case, treatment with metronidazole <24 h from presentation in our ED resulted in a positive outcome. The patient safely completed a 17-day course with no long-term neurologic sequelae noted to date.

Consent statement

Written informed consent was obtained from the patient's parent for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The authors have no funding source related to this case report to disclose.

CRediT authorship contribution statement

Mamta Shah contributed to care of the patient, evaluation of the data and literature and writing and revision of the manuscript. **Bruce Chy** contributed to care of the patient, evaluation of the data and literature and writing and revision of the manuscript. **Nathan Price** contributed to care of the patient, evaluation of the data and literature and writing and revision of the manuscript as well as supervision of **Mamta Shah** and **Bruce Chy**.

Conflict of interest statement

The authors have no conflicts of interest to disclose.

References

[1] Long S, Prober C, Fischer M, editor. Principles and practice of pediatric infectious diseases, 5th ed.; 2018.

[2] Kalay GN, Dalgic N, Bozan T, Ulger-Toprak N, Bayraktar B, Soyletir G. Polymicrobial anaerobic meningitis caused by Bacteroides fragilis, Bacteroides thetaiotaomicron, Fusobacterium necrophorum and Slackia exigua in a patient with mastoiditis following otitis media. Anaerobe 2019;56:95–7. https://doi.org/10.1016/j.anaerobe.2019.02.003. Epub 2019 Feb 14.

[3] de A, Silva C, Dias L, Cardona RSB, Variane GFT, do Nascimento SD, et al. Anaerobic neonatal meningitis: a diagnostic challenge. Anaerobe 2020;61:102134. https://doi.org/10.1016/j.anaerobe.2019.102134. Epub 2019 Dec 5.

[4] Ziebold C. Delayed etiologic diagnosis of meningitis in an extremely low birth weight newborn. Pediatr Infect Dis J 2010;383(4):388–9. https://doi.org/10.1097/INF.0b013e3181d58216.

[5] Aucher P, Saunier JP, Grollier G, Sebald M, Fauchère JL. Meningitis due to enterotoxigenic Bacteroides fragilis. Eur J Clin Microbiol Infect Dis 1996;15(10):820–3. https://doi.org/10.1007/BF01701527.

[6] Brook I. Anaerobic meningitis in an infant associated with pilonidal cyst abscess. Clin Neurol Neurosurg 1985;87(2):131–2. https://doi.org/10.1016/0303-8467(85)90111-8.

[7] Cooke RW. Bacteroides fragilis septicaemia and meningitis in early infancy. Arch Dis Child 1975;50(3):241–3. https://doi.org/10.1136/adc.50.3.241. PMID: 1147659; PMCID: PMC1544495.

[8] Feder Jr HM. Bacteroides fragilis meningitis. Rev Infect Dis 1987;9(4):783–6. https://doi.org/10.1093/clinids/9.4.783.

[9] Martínez E, Domingo P, Cadafalch J, Coll P. Mixed bacterial meningitis associated with CSF leak. Clin Infect Dis 1992;14(6):1263. https://doi.org/10.1093/clinids/14.6.1263.

[10] Odugbemi T., Jatto S.A., Afolabi K. , Bacteroides fragilis meningitis. J Clin Microbiol. 1985; 21(2), 282–83. Available from: ⟨https://doi.org/10.1128/jcm.21.2.282-283⟩.

[11] Bennett J. (Ed) 2020. Mandell, Douglas, and Bennett's principles and practice of infectious diseases, 9th ed.

[12] Nagy E, Urbán E, Sóki J, Terhes G, Nagy K. The place of molecular genetic methods in the diagnostics of human pathogenic anaerobic bacteria. A minireview. Acta Microbiol Immunol Hung 2006;53(2):183–94. https://doi.org/10.1556/AMicr.53.2006.2.5.

[13] Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH, editors. Red Book: 2021–2024: report of the committee on infectious diseases; 2021.

[14] Farah S, Alshehri MA, Alfawaz TS, Ahmad M, Alshahrani DA. *Bacteroides fragilis* meningitis in a Saudi infant: case report and literature review. Int J Pediatr Adolesc Med 2018;5(3):122–6. https://doi.org/10.1016/j.ijpam.2018.05.003. Epub 2018 Sep 18. PMID: 30805546; PMCID: PMC6363260.