



Case report

Primary meningitis due to *Fusobacterium nucleatum* successfully treated with ceftriaxone in a healthy adult male



Trager Hintze^{a,*}, Michelle Steed^{b,c}, Eric Sievers^c, John T. Bagwell^d, Nicola Selfa^e

^a Department of Pharmacy Practice, The University of Oklahoma College of Pharmacy, 1110 N. Stonewall Ave., Oklahoma City, OK, 73117, USA

^b Department of Pharmacy Practice, Idaho State University College of Pharmacy, 921 S. 8th Ave, Stop 8333, Pocatello, ID, 83209-8333, USA

^c Department of Pharmacy, Eastern Idaho Regional Medical Center, 3100 Channing Way, Idaho Falls, ID, 83404, USA

^d Department of Medicine, Eastern Idaho Regional Medical Center, 3100 Channing Way, Idaho Falls, ID, 83404, USA

^e Department of Microbiology, Eastern Idaho Regional Medical Center, 3100 Channing Way, Idaho Falls, ID, 83404, USA

ARTICLE INFO

Article history:

Received 19 June 2019

Received in revised form 3 August 2019

Accepted 3 August 2019

Keywords:

Bacterial meningitis

Fusobacterium infections

Fusobacterium nucleatum

Ceftriaxone

ABSTRACT

Fusobacterium nucleatum is a rod-shaped gram-negative obligate anaerobe; this organism, and other anaerobes, are usually not a part of the culture performed for a cerebrospinal fluid (CSF) sample. To date, four cases of *Fusobacterium* meningitis in adults have been published. We report successful treatment of a case of primary meningitis due to *Fusobacterium nucleatum* in an otherwise healthy 72-year-old male.

© 2019 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Part of the normal flora of the oropharyngeal, gastrointestinal, and female genital tracts, *Fusobacterium nucleatum* is a rod-shaped gram-negative obligate anaerobe. As a pathogen, it typically causes local infections like pharyngitis, tonsillitis, and mastoiditis. When *F. nucleatum* results in a severe bacteremic illness it is referred to as “necrobacillosis.” As a result of the bacteremia, it can cause central nervous system complications including meningitis, brain abscess, and sinus venous thrombosis [1].

Bacterial meningitis in adults is most commonly due to *Streptococcus pneumoniae*, *Listeria monocytogenes*, and *Neisseria meningitidis*. Most documented *Fusobacterium* meningitis cases occur in the pediatric population, and the majority are secondary to another infection, most commonly acute otitis media (AOM) [1–6]. Three documented cases of meningitis due to *Fusobacterium* in adults have been reported, all of which are secondary to another primary diagnosis (AOM, spinal cord injury, and cavernous venous thrombosis) [7–9]. One other case described an otherwise healthy adult with meningitis due to *F. necrophorum* and focused on the identification of the organism through polymerase chain reaction (PCR) followed by electrospray ionization mass spectrometry [10].

This case details the process of organism identification and treatment of a patient with primary meningitis due to *F. nucleatum*.

Case

A 72-year-old male presented to a regional medical center in a rural area of the United States with a 6-week history of headaches and neck pain and a 5-day history of nausea, vomiting, intractable hiccups, delirium, sixth cranial nerve palsy, hallucinations, and no history of rhinorrhea in that timeframe. The patient had a remote history of pituitary adenoma and transphenoidal resection and a carotid artery stenosis from the radiation. Lumbar puncture was performed with an elevated opening pressure. CSF was noted to be yellow and cloudy with a white blood cell count of 8955 cells/ μ L, a protein level of 400 mg/dL, and a glucose level <1 mg/dL. Computed tomography (CT) without contrast of the head was normal. The patient was initiated on a broad-spectrum antimicrobial regimen including: acyclovir, fluconazole, vancomycin, ampicillin, and ceftriaxone. Although the CSF parameters strongly indicated a bacterial course, acyclovir and fluconazole were initiated as part of the initial empiric antimicrobial regimen due to the severity of patient symptoms on arrival and the physician’s desire to broadly cover for pathogens. Prior to initiation of antimicrobials the patient was given a one-time dose of dexamethasone. Mental status showed minimal improvement 24 h following admission. At 48 h, the patient’s mental status showed marked improvement but a causative organism was yet to

* Corresponding author.

E-mail addresses: trager-hintze@ouhsc.edu (T. Hintze), iviemich@isu.edu (M. Steed), eric.sievers@hcahealthcare.com (E. Sievers).

Table 1
Treatment and Outcomes in *Fusobacterium* meningitis.

Primary Diagnosis	Otitis Media [7]	Spinal cord injury [8]	Carotid artery stenosis [9]	PCR- Electropray [10]	Meningitis(Current Case)
Empiric antimicrobial therapy	Ceftriaxone	Cefotaxime	Cefotaxime	Vancomycin	Ceftriaxone
<i>Fusobacterium</i> therapy	Vancomycin Ampicillin Metronidazole	Fosfomycin Metronidazole	Chloramphenicol Metronidazole*	Meropenem Meropenem	Vancomycin Ampicillin Ceftriaxone
Days from admission to <i>Fusobacterium</i> therapy	Penicillin 9	None reported	9	56	N/A
Adjunctive therapies	Dexamethasone	None reported	None reported	None Reported	Dexa-methasone
Outcome	Died on day 12 from increased intracranial pressure and brain stem infarction	Survived with complete symptom resolution	Survived with majority symptom resolution upon discharge	Survived with majority of symptom resolution within 12 months	Survived with majority of symptom resolution upon discharge

be identified as culture of the CSF had yielded both a negative Gram stain and negative culture. At 72 h following admission only the sixth cranial nerve palsy remained and the patient had a slightly delayed response to questioning; otherwise the patient's mental status continued to improve. A sample was sent to the University of Washington Molecular Diagnostics Laboratory (UW-MDL) for PCR DNA amplification. The organism *F. nucleatum* was unequivocally identified with broad-range PCR, bacterial 16S rRNA gene primers. This result allowed a diagnosis of meningitis due to *F. nucleatum* on day six. On day eight, the patient was transferred to a skilled nursing facility (SNF) and continued on ceftriaxone as the sole antimicrobial agent for an additional 14 days.

The patient finished the course of antimicrobials at the SNF and was discharged home. A repeat lumbar puncture was not performed as the patient had a complete resolution of symptoms. An infectious disease physician followed up with the patient via telephone at SNF discharge and 10 months. The patient declined an office visit and full workup, but reported a complete resolution of symptoms.

Discussion

Differing from the majority of other documented *Fusobacterium* infections, this case has no clear source of infection and appeared to be primary in origin. In the four previously reported cases, infection with *Fusobacterium* was fatal in one of the four patients. The patient in the fatal case report had an extensive history of alcoholism with encephalitis and hydrocephalus complicating the clinical course and failed to respond to combination metronidazole and penicillin [7]. In all cases, the identification of the bacterium via CSF culture was delayed, likely because anaerobic cultures are generally not performed on CSF samples [7–10]. In the current case and in three of four reported cases, patients were started on a broad empiric antimicrobial regimen for meningitis that included a third-generation cephalosporin (see Table 1) [7–9]. One case included meropenem in addition to vancomycin [10]. In surviving patients, the agent used was either cefotaxime, meropenem, or ceftriaxone (current case). The patients from the three published reports of surviving cases were treated with metronidazole only after the finding of *Fusobacterium* and responded to therapy within 48–72 h of administration. The patient described in the current case was not changed from ceftriaxone because of the marked improvement demonstrated on this agent.

With no established guidelines for treatment of meningitis due to *Fusobacterium*, antibacterial selection is guided by clinical

judgement, available drug resources, and drug action. Coverage of *Fusobacterium* could have been conferred by ampicillin or ceftriaxone from the empiric regimen, though neither of these agents would be a first-line option for an anaerobe like *Fusobacterium*. In the published case reports where the patient survived, neither ampicillin or ceftriaxone was a chosen agent. Use of cefotaxime over ceftriaxone may have been entirely due to formulary restrictions; the similarities in antibacterial coverage between these two third-generation cephalosporins would suggest similar results should be expected from either agent. Ampicillin was chosen as part of the empiric therapy because of the patient's age and risk for meningitis due to *Listeria* species. The nature of the infection being primary or secondary may play a role in the efficacy of a third-generation cephalosporin. In the published cases, meningitis due to *Fusobacterium* was secondary to another disease process whereas the infection was primary in the present case.

The ability to send a sample to UW-MDL for PCR DNA amplification greatly aided the institution in the identification of a causal organism. In areas without this resource, identification is delayed, but with a focus on patient symptom improvement and a high usage rate of ceftriaxone in empiric therapy for meningitis it is possible there are other cases of meningitis due to *Fusobacterium* that are not identified. As universal PCR becomes available to a greater number of institutions, the identification of meningitis due to *Fusobacterium* could increase and ceftriaxone could be considered as a viable option for treatment.

Note

At the time of patient encounter, data collection, and article preparation Dr. Hintze was a fourth-year pharmacy student at Idaho State University College of Pharmacy.

CRedit authorship contribution statement

Trager Hintze: Data curation, Resources, Writing - original draft, Writing - review & editing. **Michelle Steed:** Writing - original draft, Supervision. **Eric Sievers:** Data curation, Writing - review & editing. **John T. Bagwell:** Data curation, Writing - review & editing. **Nicola Selfa:** Resources, Writing - review & editing.

Acknowledgements

The authors would like to thank Dr. Shanna O'Connor for her aid and guidance in preparation of the manuscript.

References

- [1] Van Munster MPE, Brus F, Mul D. Rare but numerous serious complications of acute otitis media in a young child. *BMJ Case Rep* 2013;2013: pii: bcr2012008149.
- [2] Jacobs JA, Hendriks JJ, Verschure PD, van der Wurff AM, Freling G, Vos GD, et al. Meningitis due to *Fusobacterium necrophorum* subspecies *necrophorum*. Case report and review of the literature. *Infection* 1993;21:57–60.
- [3] Angelino G, Cantarutti N, Chiurchiù S, Amodio D, De Luca M, Lancella L, et al. Fulminant *Fusobacterium necrophorum* meningitis in an immunocompetent adolescent. *Pediatr Emerg Care* 2012;28:703–4.
- [4] Le Monnier A, Jamet A, Carbonnelle E, Barthod G, Moumille K, Lesage F, et al. *Fusobacterium necrophorum* middle ear infections in children and related complications: report of 25 cases and literature review. *Pediatr Infect Dis J* 2008;27:613–7.
- [5] Jaremko JL, Kirton A, Brenner JL. A 12 year old girl with pharyngitis, meningitis and sinus venous thrombosis. *CMAJ* 2003;169:811–2.
- [6] Le Moal G, Landron C, Grollier G, Bataille B, Roblot F, Nassans P, et al. Characteristics of brain abscess with isolation of anaerobic bacteria. *Scand J Infect Dis* 2003;35:318–21.
- [7] Garimella S, Inaparthi A, Herchline T. Meningitis due to *Fusobacterium necrophorum* in an adult. *BMC Infect Dis* 2004;4:24.
- [8] Denes E, Cypierre A, Vacquier J, Matt M, Weinbreck P. Meningitis due to *Fusobacterium nucleatum* after a kart crash. *Med Mal Infect* 2013;43:486–7.
- [9] Jones TH, Bergvall V, Bradshaw JP. Carotid artery stenoses and thrombosis secondary to cavernous sinus thromboses in *Fusobacterium necrophorum* meningitis. *Postgrad Med J* 1990;66:747–50.
- [10] Nagalingam S, Lisgaris M, Rodriguez B, Jacobs MR, Lederman M, Salata RA, et al. Identification of occult *Fusobacterium nucleatum* central nervous system infection by use of PCR-electrospray ionization mass spectrometry. *J Clin Microbiol* 2014;52:3462–4.