

Fellows Column: Capnocytophaga Sepsis in a Preterm Neonate: A Case Report

Najmus Sehr Ansari MBBS, MSc, Elizabeth Asztalos MD, MSc, FRCP(C), Asaph Rolnitsky, MD, MSc

Abstract

Background: *Capnocytophaga* is an anaerobic gram-negative bacillus part of oral flora in humans, cats, and dogs. It usually causes periodontal infection but may exhibit systemic manifestations, particularly in immunocompromised individuals. In rare cases, it may cause chorioamnionitis leading to preterm birth and early-onset neonatal sepsis.

Case Presentation: We present a rare case of early-onset sepsis due to *Capnocytophaga* in an extremely preterm newborn presenting severe respiratory distress, lethargy, and leukopenia at birth. This was treated with Cefotaxime for 14 days.

Conclusion: Our case report highlights the importance of considering unusual pathogens such as *Capnocytophaga* as a cause for intra-amniotic infections leading to preterm birth and early-onset neonatal infection.

Keywords: Preterm neonate, Sepsis, Chorioamnionitis, *Capnocytophaga*, Case report

List of Abbreviations

VDRL Venereal disease research laboratory test

MRI Magnetic resonance imaging

RNA Ribonucleic acid

*“Our case report highlights the importance of considering unusual pathogens such as *Capnocytophaga* as a cause for intra-amniotic infections leading to preterm birth and early-onset neonatal infection.”*

Introduction:

Capnocytophaga is an anaerobic gram-negative bacillus that is present in commensal oral flora of humans, cats, and dogs (1). It usually causes periodontal infection but may exhibit systemic manifestations such as endophthalmitis, keratitis, endocarditis, pyelonephritis, and septic arthritis, particularly in immunocompromised individuals (2,3). It has also been reported to cause chorioamnionitis leading to preterm birth and neonatal sepsis (1,3,4,5). We describe a rare case of early-onset sepsis due to *Capnocytophaga* sputigens in a preterm neonate. This case report demonstrates the importance of considering unusual pathogens such as *Capnocytophaga* as a cause for chorioamnionitis leading to preterm birth and early-onset neonatal infection.

*“Blood culture was drawn at birth, and Ampicillin and Gentamicin were started. Microscopic evaluation of the placenta showed acute chorionic vasculitis on the fetal surface of the placenta, patchy villous edema, and focal decidual necrosis suggestive of chorioamnionitis. His initial leukocyte count was $4.1 \times 10^9/l$ with neutrophils of $0.9 \times 10^9/l$. Blood and skin swab culture showed the growth of *Capnocytophaga* sputigens after 72 hours of inoculation.”*

Case Presentation:

A male neonate weighing 527 grams was delivered to a healthy 32-year-old woman at 23 weeks of gestation. She was Rubella immune and negative for Hepatitis B surface antigen, Venereal disease research laboratory test (VDRL), Human immunodeficiency virus, Gonococci, and Chlamydia. An ultrasound scan at 18 weeks of gestation showed normal fetal anatomy. This was an uneventful pregnancy until she presented with preterm labour at 23 weeks of gestation. She received one dose of Betamethasone and Ceftriaxone prior to delivery. Her labor progressed, resulting in a spontaneous vaginal delivery. He required resuscitation followed by intubation, surfactant administration, and placement on a high-frequency oscillator ventilator at delivery. He was lethargic and had poor tone.

Blood culture was drawn at birth, and Ampicillin and Gentamicin were started. Microscopic evaluation of the placenta showed acute chorionic vasculitis on the fetal surface of the placenta, patchy villous edema, and focal decidual necrosis suggestive of chorioamnionitis. His initial leukocyte count was $4.1 \times 10^9/l$ with neutrophils of $0.9 \times 10^9/l$. Blood and skin swab culture showed the growth of *Capnocytophaga* sputigens after 72 hours of inoculation. Due to poor growth on all susceptibility testing media, antibiotic susceptibility could not be done. Lumbar puncture was deferred given clinical instability. Antibiotics were changed to Cefotaxime after consulting a pediatric infectious disease specialist. Blood culture repeated on day 5 of life showed no growth. Serial monitoring of C-reactive protein was done which was 38mg/L on day 2 of life and subsequently dropped to less than 1mg/L by day 10. He received Cefotaxime for a total duration of 14 days. His clinical course was further complicated by *Candida Albicans* sepsis and meningitis at three weeks of age. He was treated with Amphotericin B followed by oral Fluconazole for six weeks from negative culture. His abdominal ultrasound, eye exam, and brain MRI were negative for fungal lesions. Serial cranial ultrasounds

showed bilateral subependymal and intraventricular hemorrhages, which resolved at 34 weeks of corrected gestational age. He was discharged home on oxygen support at 44+2 weeks of age. He came off oxygen support three months after discharge. His neurodevelopmental follow-up at eight months of corrected age showed normal milestones for his age, and he continues to be monitored in our follow-up clinic.

“Capnocytophaga is present in the human oropharynx as a commensal flora (2). In the susceptible individual, it has been postulated that proteolytic enzymes produced by these bacteria damage the oral mucosal barrier providing a route of entry into the bloodstream (6). The hematogenous spread to the placenta in the pregnant patient may result in chorioamnionitis (2,6).”

Discussion:

Capnocytophaga is present in the human oropharynx as a commensal flora (2). In the susceptible individual, it has been postulated that proteolytic enzymes produced by these bacteria damage the oral mucosal barrier providing a route of entry into the bloodstream (6). The hematogenous spread to the placenta in the pregnant patient may result in chorioamnionitis (2,6). Another possible route can be an ascending infection through the cervix after urogenital contact from a partner with periodontitis (1,7). With chorioamnionitis, there is an activation of proinflammatory cytokines and production of prostaglandin, which may trigger premature uterine contractions and degradation of the amniotic membrane leading to preterm birth (8-10).

Capnocytophaga species appear as thin fusiform gram-negative rods on gram staining. They require a carbon dioxide-enriched culture medium for their growth. Owing to this property and being slow in growth, their identification on routine culture media can often be difficult (2). However, molecular methods such as 16S ribosomal RNA gene polymerase chain reaction and sequencing can be used for rapid and accurate detection of this bacteria (1). Capnocytophaga species show susceptibility to third-generation cephalosporins, lincosamides, carbapenems, macrolides, and fluoroquinolones but are generally resistant to aminoglycosides, trimethoprim, and metronidazole (6).

Neonatal infection with Capnocytophaga is rare, with only a few cases reported in the medical literature. A current search in the literature revealed 27 reported cases of Capnocytophaga neonatal infection (1,3,10,11,12). Most of these neonates, 26/27, were delivered preterm with 19 less than 30 weeks gestation. All the mothers presented with symptoms suggestive of chorioamnionitis and preterm labor except one who presented with placental abruption (3). Most of these infants were treated with Ampicillin; however, four neonates were treated with Cefotaxime (3,7). Combination

therapy was used in three neonates: Amoxicillin-Clavulanate in one (1) and Ampicillin, Cefotaxime, and Gentamicin in the other two infants (2). In our case, the mother presented with preterm labor with the infant presenting with signs of early-onset sepsis manifested by severe respiratory distress, lethargy, and leukopenia. This was treated with a 14-day course of Cefotaxime resulting in an effective eradication of this infection. However, he had complications related to prematurity which significantly impacted his clinical course in NICU. Our case and previously reported cases indicate that neonatal infections due to Capnocytophaga are usually not severe as they are highly susceptible to antimicrobial therapy (7). However, morbidity may increase significantly owing to premature delivery resulting from chorioamnionitis (2).

Conclusion:

“Our report demonstrates the importance of not only considering urogenital commensals but also the microbiota from distant sites as a potential etiology for chorioamnionitis leading to preterm birth and neonatal infection. This knowledge may guide clinicians in implementing therapeutic strategies which could potentially prevent preterm labor and early-onset neonatal sepsis.”

The infectious etiology of preterm birth remains the leading cause of neonatal morbidity and mortality. An improved understanding of bacterial organisms and their route of invasion is obligatory to make progress in preventing preterm birth, which is a significant public health concern. The role of urogenital flora in causing chorioamnionitis is extensively studied, but much less is known about other bacterial populations causing intra-amniotic infection. Our report demonstrates the importance of not only considering urogenital commensals but also the microbiota from distant sites as a potential etiology for chorioamnionitis leading to preterm birth and neonatal infection. This knowledge may guide clinicians in implementing therapeutic strategies which could potentially prevent preterm labor and early-onset neonatal sepsis. Further research is required to understand better its role in causing chorioamnionitis leading to preterm birth.

References:

1. Felix L, Rosenberg A, Caraballo KA, et al. Capnocytophaga spp. infection causing chorioamnionitis: an unusual suspect. Anaerobe. 2019 Oct;59:115-117. doi: 10.1016/j.anaerobe.2018.07.006. Epub 2018 Jul 19. PMID: 30031140.
2. Mekouar H, Voortman G, Bernard P et al. Capnocytophaga species and perinatal infections: case report and review of the literature. Acta Clin Belg. 2012 Jan-Feb;67(1):42-5. doi: 10.2143/ACB.67.1.2062626. PMID: 22480039.
3. Marsicek SM, Berman D. Neonatal Bacteremia Caused by an Unusual Suspect. Clin Pediatr (Phila). 2017 Sep;56(10):971-

974. doi: 10.1177/0009922817706149. Epub 2017 Apr 24. PMID: 28436238.
4. Edwards C, Yi CH, Currie JL. Chorioamnionitis caused by *Capnocytophaga*: case report. *Am J Obstet Gynecol*. 1995 Jul;173(1):244-5. doi: 10.1016/0002-9378(95)90207-4. PMID: 7631698.
 5. Douvier S, Neuwirth C, Filipuzzi L, et al. Chorioamnionitis with intact membranes caused by *Capnocytophaga sputigena*. *Eur J Obstet Gynecol Reprod Biol*. 1999 Mar;83(1):109-12. doi: 10.1016/s0301-2115(98)00240-1. PMID: 10221619.
 6. Chan E, Mildenhall L, Taylor S. A rare case of early-onset neonatal sepsis. *JMM case reports*. 2014 Sep 1;1(3):e001099.
 7. Lopez E, Raymond J, Patkai J, et al. *Capnocytophaga* species and preterm birth: case series and review of the literature. *Clin Microbiol Infect*. 2010 Oct;16(10):1539-43. doi: 10.1111/j.1469-0691.2009.03151.x. PMID: 20041890.
 8. Park JS, Park CW, Lockwood CJ, et al. Role of cytokines in preterm labor and birth. *Minerva Ginecol*. 2005 Aug;57(4):349-66. PMID: 16170281.
 9. Mendz GL, Kaakoush NO, Quinlivan JA. Bacterial aetiological agents of intra-amniotic infections and preterm birth in pregnant women. *Front Cell Infect Microbiol*. 2013 Oct 16;3:58. doi: 10.3389/fcimb.2013.00058. PMID: 24137568; PMCID: PMC3797391.
 10. Hopkins AM, Desravines N, Stringer EM, Zahn K, Webster CM, Krajick K, Vora NL. *Capnocytophaga* bacteremia precipitating severe thrombocytopenia and preterm labor in an asplenic host. *Infect Dis Rep*. 2019 Dec 5;11(3):8272. doi: 10.4081/idr.2019.8272. PMID: 31857872; PMCID: PMC690230

Consent for publication: Written informed consent was obtained from the patient's parents to publish this case report.

Competing interests: The authors declare that they have no competing interests.

Funding: No funding received from any public, commercial, or non-profit organization.

Authors' contributions: NSA, EA, and AR conceptualized writing this case report. NSA drafted the initial manuscript, which AR and EA revised. NSA conducted the literature review for this case study. AR and EA supervised the literature review, critically reviewed the manuscript, and approved the final version.

Conflicts of Interest: The author has no conflicts of interest relevant to this article to disclose.

NT

Corresponding Author



Najmus Sehr Ansari MBBS, MSc
Clinical Fellow – Perinatal Neonatal Medicine, University of Toronto
Sunnybrook Health Sciences Centre
2075 Bayview Avenue, M Wing
Toronto, Ontario M4N 3M5, Canada
Contact number: +1 (647) 892 5381
E-mail: sehr.ansari@sickkids.ca



Elizabeth Asztalos MD, MSc, FRCP(C)
Professor of Pediatrics, University of Toronto
Sunnybrook Health Sciences Centre
2075 Bayview Avenue, M Wing
Toronto, Ontario M4N 3M5, Canada
E-mail: Elizabeth.asztalos@sunnybrook.ca



Asaph Rolnitsky MD, MSc
Assistant Professor of Pediatrics, University of Toronto
Sunnybrook Health Sciences Centre
2075 Bayview Avenue, M Wing
Toronto, Ontario M4N 3M5, Canada
E-mail: asaph.rolnitsky@sunnybrook.ca

NEONATOLOGY TODAY is interested in publishing manuscripts from Neonatologists, Fellows, NNPs and those involved in caring for neonates on case studies, research results, hospital news, meeting announcements, and other pertinent topics.

Please submit your manuscript to: LomaLindaPublishingCompany@gmail.com

Fellow's Column is published monthly.

- Submission guidelines for "Fellow's Column":
- 2000 word limit not including references or title page. Exceptions will be made on a case by case basis
- QI/QA work, case studies, or a poster from a scientific meeting may be submitted..
- Submission should be from a medical student, resident, fellow, or NNP in training.
- Topics may include Perinatology, Neonatology, and Younger Pediatric patients.
- No more than 20 references.
- Please send your submissions to:

Elba Fayard, MD, Interim Fellowship Column Editor
or Japmeet Sandhu, OMS III, Fellowship Column Assistant Editor
LomaLindaPublishingCompany@gmail.com