Mycoplasma hominis meningitis in an extremely preterm newborn: a case report

Najmus Sehr Ansari*, Elizabeth Asztalos and Asaph Rolnitsky

Abstract

Background: Mycoplasma Hominis is a micro-organism which is a part of the human genitourinary tract flora. Neonates are susceptible to acquire this pathogen either in utero or through vertical transmission. In rare cases, it may cause central nervous system infections with severe morbidity and mortality in preterm and term neonates.

Case presentation: We present a case of Mycoplasma Hominis meningitis in an extremely preterm neonate who presented with lethargy, tachycardia and seizures on day 7 of life. There was no history of maternal systemic or genitourinary infection during pregnancy and at the time of delivery. Empirical antibiotic therapy for neonatal meningitis was commenced after sending blood and cerebrospinal fluid cultures. Cerebrospinal fluid analysis showed pleocytosis with neutrophilic predominance, but no bacteria was identified on gram staining. Blood culture yielded no growth of any bacterial pathogen. However, growth of Mycoplasma Hominis was suspected in cerebrospinal fluid culture which was confirmed by 16S ribosomal ribonucleic acid (RNA) polymerase chain reaction analysis. Subsequently, antibiotics were changed to Moxifloxacin and Doxycycline which were given for a total duration of 6 weeks. Multiple cerebrospinal fluid cultures were performed during this treatment. No growth of any pathogen was identified on any of these cerebrospinal fluid cultures.

Conclusions: We report a rare case of Mycoplasma Hominis meningitis in an extremely preterm neonate which was successfully treated with a combination therapy of Moxifloxacin and Doxycycline. It is important to consider the possibility of Mycoplasma Hominis meningitis in neonates who present with clinical signs and pleocytosis in cerebrospinal fluid but negative gram staining and no growth on conventional culture media.

Keywords: Preterm neonate, Meningitis, Mycoplasma Hominis, Case report

Background

Mycoplasma Hominis is a frequent inhabitant of the human genital tract [1]. Neonates are susceptible to acquire this microbe either in utero or through the colonized birth canal during the process of parturition [2]. However, invasive infections with this organism in preterm and term infants are noted to be rare [1, 3]. We describe an unusual case of neonatal meningitis due to Mycoplasma Hominis, confirmed in bacterial cultures and 16s ribosomal RNA Polymerase chain reaction (PCR) analysis. This case report demonstrates the importance of suspecting Mycoplasma Hominis as a cause of central nervous system (CNS) infection in neonates who present with clinical signs but no growth on conventional bacterial cultures and no improvement on empirical antibiotic treatment.

Case presentation

A male neonate was born at 25 + 6 weeks of gestation to 35 years old gravida 2, parity1 (G2P1) mother with anti-phospholipid antibody syndrome. This was an in vitro fertilization (IVF) pregnancy. She was Rubella immune
and negative for Hepatitis B surface antigen, Venereal disease research laboratory test (VDRL), Human immunodeficiency virus, Gonococci and Chlamydia. Her urine culture and vaginal swab for Group B Streptococci was also negative. Her anatomy scan at 18 weeks of gestation showed normal fetal anatomy and a short cervix for which she underwent cervical cerclage placement at 20+5 weeks gestation. There was no history of chorioamnionitis or prolonged rupture of membranes. She presented at 25+5 weeks with preterm labor and had a spontaneous vaginal delivery the next day. She had received two doses of Betamethasone and Magnesium sulphate prior to delivery. He initially required positive pressure ventilation followed by intubation and surfactant administration with an acceptable response. Umbilical arterial and venous catheters were placed and the neonate was transferred to neonatal intensive care unit (NICU) in a stable condition.

A blood culture was drawn at birth and empiric treatment with Ampicillin and Gentamicin was initiated. The antibiotics were discontinued after 36 hours as the blood culture showed no growth and he remained clinically stable. In addition, as per unit protocol, an endotracheal aspirate was sent for a Ureaplasma culture on admission. This grew a Mycoplasma species for which 3 days of antibiotics were started as empiric antibiotics. His CSF cultures was completed and Vancomycin and Cefotaxime were started as empiric antibiotics. His CSF analysis showed red blood cells (RBC) count of 4887 × 10E6/l, protein 3691 mg/l and glucose 0.5 mmoles/liter. No growth was seen on any of these CSF cultures. Antibiotics were then changed to Moxifloxacin and Doxycycline. The repeat CSF culture after 48 hours of Moxifloxacin and Doxycycline showed no growth. CSF analysis done seven days after starting this treatment showed RBC 5650 × 10E6/l, WBC 449 × 10E6/l, protein 3763 mg/l and glucose 0.2 mmoles/liter. Subsequent CSF findings repeated after another three days showed further improvement, RBC 7187 × 10E6/l, WBC 93 × 10E6/l, protein 3691 mg/l and glucose 0.5 mmoles/liter. No growth was seen on any of these CSF cultures. Serial head ultrasound scans were done which showed progressive ventriculomegaly, post hemorrhagic ventricular dilatation and cystic evolution of hemorrhagic/venous infarct in the right frontoparietal region. Although these findings could be attributed to extreme prematurity; there is a likelihood that infection with Mycoplasma Hominis may have played a role in its progression. There have been documented cases of Mycoplasma Hominis meningitis resulting in CNS complications including intraventricular and periventricular hemorrhage, hydrocephalus, and infarction [3]. Lumbar taps were repeated as therapeutic measure to reduce ventriculomegaly, but optimal volumes of CSF were not obtained. Because of the ventriculomegaly, he was evaluated for a possible shunt on day 31; this was deferred because of the stable ventriculomegaly.

Antibiotics were given for a total duration of six weeks after which he was discharged home with a normal neurological examination. He was referred to Neurodevelopmental clinic for follow-up.

Discussion and conclusion
Neonatal CNS infections with Mycoplasma Hominis, although rare, can cause severe morbidity and mortality in neonates [1]. In a case series of 29 neonates with Mycoplasma Hominis infection (age of presentation day1-32 of life), Hata and colleagues reported complications such as brain abscess, hydrocephalus, infarction, cerebritis and periventricular/intraventricular hemorrhage in 34 % cases, death in 28 % and sequelae mostly hemiparesis in another 28 % cases [3]. This may be attributed to a delay in diagnosis, ineffective antibiotic treatment, or suboptimal treatment regimens for neonatal CNS disease [3, 4]. Therefore, prompt diagnosis, early initiation and optimal duration of appropriate antibiotic therapy is necessary for a favorable prognosis.

The clinical presentation may include apnea, temperature instability, lethargy, vomiting, irritability poor tone, twitching or seizures [7]. Detection of Mycoplasma Hominis can be challenging since they lack peptidoglycan cell wall which renders them unidentifiable by gram staining [5]. In addition to this, they grow very slowly on routine culture media and require a specific blood agar medium for their detection [1, 6]. Due to this,
there is a likelihood that Mycoplasma Hominis infections may remain undiagnosed or diagnosed late in infants presenting with clinical signs and symptoms [2]. Hence, it is important to consider the possibility of Mycoplasma Hominis infection in cases where the CSF shows pleocytosis and no growth of organism on routine culture media. A 16S ribosomal RNA PCR analysis has proven useful for detection of Mycoplasma Hominis in blood and CSF which are difficult to grow on standard culture media [7, 8]. The microbe is identified by direct sequencing analysis after amplification by PCR. Use of pathogen-specific primers in 16S RNA analysis results in rapid detection of the specific organism [4]. Prematurity, low birth weight, and neural tube defects are recognized to be the most common risk factors for neonatal meningitis with Mycoplasma Hominis [6]. However, it has also been seen in term neonates with no neurological birth malformations [1, 3].

The treatment options for Mycoplasma Hominis meningitis and its duration remains unclear [1, 9]. Due to the rarity of this infection in neonates, the current recommendations are based on clinical experiences and in-vitro susceptibility test results [9, 10].

Mycoplasma Hominis has shown susceptibility to Chloramphenicol, Tetracyclines, Lincosamide and Fluoroquinolones in in-vitro testing [11]. Fluoroquinolones have been used in past to treat neonatal mycoplasma hominis meningitis successfully [1, 3, 5]. Moxifloxacin, a fourth-generation fluoroquinolone is preferred because of its ability to concentrate in CSF and its bactericidal effects in CNS infections [1, 12, 13]. Although there are cases which were successfully treated with Moxifloxacin monotherapy [1, 6], there is a risk of development of resistance with fluoroquinolones during treatment [9, 14, 15]. Our literature search revealed only two reported cases of neonates who were given Moxifloxacin in combination with another antibiotic for Mycoplasma Hominis meningitis [3, 5] (Table 1).

Evidence from previously published cases show that 28% neonates with Mycoplasma Hominis CNS infection died whereas 34% had some CNS complications and 28% cases developed some neurological sequelae mostly hemiparesis [3]. In our case, treatment with a combination therapy of Moxifloxacin and Doxycycline resulted in significant clinical and laboratory improvement in terms of negative CSF culture after 48 hours of initiating this regimen and decreased WBC count and protein in subsequent CSF analysis. Our patient was discharged home with a normal neurological examination and stable ventriculomegaly. His neurodevelopmental follow up at six months of age showed normal neurological findings.

It is important to consider Mycoplasma Hominis as a potential cause for neonatal meningitis in infants particularly those with previous colonization with this rare but devastating species. Our case demonstrates effective eradication of Mycoplasma Hominis with a combination therapy of Moxifloxacin and Doxycycline. However, further research is required to understand the pharmacokinetics of these antibiotics to establish optimal dosing and duration for effective treatment of CNS infections with Mycoplasma Hominis.

Table 1 Characteristics of neonates treated with combination therapy (Moxifloxacin and another antibiotic) for Mycoplasma Hominis CNS infection

| Age at presentation | Confirmation of diagnosis | Empirical antibiotic and duration | Antibiotics for Mycoplasma Hominis | Outcome |
|---------------------|--------------------------|----------------------------------|-----------------------------------|---------|
| Hata and colleagues³ | 16S RNA PCR (day 1–2) Ciprofloxacin (day 6–17) Acyclovir (day 6–8) Chloramphenicol (day 8–17) | Minocycline for 28 days (day 6–34) Moxifloxacin for 17 days (day 17–34) | Recovery with left hemiplegia |
| Watt and colleagues⁵ | 16S RNA PCR (day 1–8) Ceftazidime (day 1–5) Vancomycin (day 8–19) Acyclovir (day 8–19) Meropenem (day 12–19) | Doxycycline for 6 weeks (day 19–60) Moxifloxacin for 6 weeks (day 19–60) | Recovery, neurological outcomes not reported |
| Our case | 16S RNA PCR (day 1–2) Azithromycin (day 3–6) Vancomycin and cefotaxime (day 7–10) | Doxycycline for 6 weeks (day 10–52) Moxifloxacin for 6 weeks (day 10–52) | Recovery with normal neurological examination at discharge, follow up at 6 months showed normal neurological examination |

Abbreviations
G2P1: Gravida2, Parity1; PCR: Polymerase chain reaction; RNA: Ribonucleic acid; IVF: In vitro fertilization; CSF: Cerebrospinal fluid;
RBC: Red blood cells; WBC: White blood cells; CNS: Central nervous system; VDRL: Venereal disease research laboratory test; NICU: Neonatal intensive care unit

Acknowledgements
Not applicable.

Authors’ contributions
NSA, EA, and AR conceptualized the idea of writing this case report. NSA drafted the initial manuscript which was revised by AR and EA. AR and EA supervised the literature review for this case study, critically reviewed the manuscript, and approved the final version.

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

Availability of data and materials
Not applicable.

Ethics approval and consent to participate
None.

Consent for publication
Written informed consent was obtained from patient’s parents for publication of this case report.

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

Received: 30 September 2020 Accepted: 2 February 2021
Published online: 08 February 2021

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