Case report of a 6-year-old girl with *Mycoplasma hominis* ventriculoperitoneal shunt infection

Masanori Sato, MD,¹ Noriko Kubota, PhD,² Yoshihiko Katsuyama, PhD,³ Yota Suzuki, MD,⁴ Yosuke Miyairi, MD,⁴ Kisei Minami, MD,⁵ and Masashi Kasai, MD¹

Departments of ¹Pediatric Intensive Care, ²Laboratory Medicine, ⁴Neurosurgery, and ⁵General Pediatrics, Nagano Children's Hospital; and ³Department of Pharmacy, Shinshu University Hospital, Nagano, Japan

Mycoplasma hominis is a rare causative pathogen for surgical site infections after neurosurgical procedures. This organism lacks a cell wall, rendering it undetectable by Gram staining and making it resistant to beta-lactam antibiotics. In addition, some special techniques are required to identify this organism. Thus, it is very difficult to diagnose infections caused by this pathogen. Here, the authors report a pediatric case of *M. hominis* ventriculoperitoneal shunt (VPS) infection with central nervous system involvement for which beta-lactam antibiotics were not effective and Gram staining revealed no pathogens. Because few cases have been described that involve the treatment of *M. hominis* infection after neurosurgery, in this case the patient's serum and CSF were monitored for antibiotic drug concentrations. Successful treatment of the infection was achieved after approximately 6 weeks of administration of clindamycin and ciprofloxacin antibiotics in addition to external ventricular drain revision and subsequent VPS replacement. When beta-lactam antibiotics are ineffective and when Gram staining cannot detect the responsible pathogens, it is important to consider *M. hominis* as the atypical pathogen.

<https://thejns.org/doi/abs/10.3171/2017.1.PEDS16520>

KEY WORDS *Mycoplasma hominis*; ventriculoperitoneal shunt infection; Gram staining; central nervous system infection

Mycoplasma hominis is a small prokaryotic organism belonging to the genus *Mycoplasma*. This organism lacks a cell wall, rendering it undetectable by Gram staining and making it resistant to beta-lactam antibiotics. Unlike other *Mycoplasma* species, *M. hominis* can grow on blood agar and chocolate agar plates; however, such growth is very slow and special techniques are required to identify this organism. Thus, it is very difficult to diagnose infections caused by this pathogen.⁴ *M. hominis* most commonly colonizes the urogenital tracts of sexually active adults and can be a causative agent of their urogenital tract infections. In pediatric populations, this organism is sometimes associated with invasive neonatal infections^{5,8,20,22} due to the acquisition of the microbe from a colonized birth canal, although asymptomatic colonization has also been reported.^{16–19} However, invasive infections by *M. hominis* after the neonatal period are very rare. In the

past, this organism has been reported as a potential cause of some severe childhood infections following the neonatal period,^{6,7,9,13} including a few invasive cases with central nervous system (CNS) involvement.^{10,21} Although previous reports have suggested that immunosuppression may play a role in cases of extragenital infection caused by *M. hominis*,^{11,21} there are no known risk factors for *M. hominis* infection and immunocompetent children can be infected by the organism. Because of the low number of reported cases, the standard antibiotic regimen for CNS infection caused by *M. hominis* is undetermined. In addition, there have been only a few reports of device-related infections associated with this organism and the optimal regimen for the management of such infections remains unknown.

Here, we present a successfully treated case of ventriculoperitoneal shunt (VPS) infection with CNS involvement caused by *M. hominis*.

ABBREVIATIONS CNS = central nervous system; ETV = endoscopic third ventriculostomy; EVD = external ventricular drain; MIC = minimum inhibitory concentration; PCR = polymerase chain reaction; SSI = surgical site infection; VPS = ventriculoperitoneal shunt.

SUBMITTED September 12, 2016. **ACCEPTED** January 18, 2017.

INCLUDE WHEN CITING Published online March 3, 2017; DOI: 10.3171/2017.1.PEDS16520.

Case Report

A 6-year-old girl with hydrocephalus resulting from aqueductal stenosis underwent VPS insertion. She had undergone endoscopic third ventriculostomy (ETV) 6 months previously; however, follow-up MRI revealed re-obstruction of her third ventricle floor. Because fenestration of her third ventricle floor on the first ETV had been difficult due to its anatomical limitations, repeat ETV was not considered. The patient also had a diagnosis of pan-hypopituitarism and was taking hydrocortisone at 0.25 mg/kg/day. Cefazolin was administered for prophylaxis of surgical site infection (SSI) until her 5th postoperative day. Although transient fever was observed for a few days during her hospitalization, no symptoms of the SSI were observed and the fever subsided without treatment. The patient appeared to have recovered completely and was subsequently discharged on her 8th postoperative day. However, 2 days after discharge, she returned with intermittent fever and was readmitted into our hospital.

Upon readmission, the patient had a fever of 38.4°C but was alert, with good tissue perfusion and without headache. The abdominal incision was erythematous (Fig. 1), and the skin overlying the VPS on the left side of the pa-

tient's head was slightly swollen. Her abdomen was soft and flat. A sepsis workup was performed, including blood and CSF cultures. Laboratory data upon her readmission were as follows: leukocytes, $16.5 \times 10^9/L$; C-reactive protein, 48.7 mg/L; and blood glucose, 5.5 mmol/L. Other values remained normal. CSF analysis revealed $33.0 \times 10^6/L$ leukocytes with 31% polynuclear cells, a protein value of 90.0 mg/L, and a glucose level of 3.4 mmol/L. Although no microorganisms were detected by Gram staining of the CSF, treatment with intravenous vancomycin plus ceftazidime was empirically started for suspected meningitis and VPS infection. On the same day, the VPS was initially externalized in the operating theater. At that time, a small amount of pus was drained from the abdominal incision. Gram staining of the pus also failed to reveal any microorganisms.

The patient remained febrile for 3 days despite the administration of antibiotics and externalization of the VPS, but blood and CSF cultures performed upon her readmission appeared to be negative. On her 4th day in the hospital, however, the sample of pus obtained from the abdominal incision grew pinpoint colonies on both blood agar and chocolate agar plates (Fig. 2). Because Gram staining of the colonies failed to reveal microorganisms, atypical organisms were assumed to be causative pathogens. We thus used 16S ribosomal RNA sequencing to identify the isolate responsible, as previously described.¹² Eventually, the isolate was identified as *M. hominis*. Subsequently, the intravenous antibiotics were changed to ciprofloxacin (10 mg/kg every 12 hours) plus clindamycin (13 mg/kg every 8 hours) on the patient's 6th day in the hospital. Soon after this change of the antibiotic regimen, the

FIG. 1. Image showing the patient's abdomen with redness around the incision site. Figure is available in color online only.

FIG. 2. Image showing pinpoint colonies grown from a pus sample on a chocolate agar plate. Pinpoint colonies grew from pus samples on both blood agar and chocolate agar plates. At a later date, the same type of colonies also grew from CSF samples. Figure is available in color online only.

fever subsided. On the patient's 11th day in the hospital, the CSF sample obtained upon her readmission also grew colonies of *M. hominis*, indicating that the organism had also caused meningitis. Antibiotic administration was continued and CSF and serum were monitored for drug concentrations. Cultures and polymerase chain reaction (PCR) assays, using specific primers for *M. hominis* as previously described,³ were repeated for CSF samples on the patient's 5th, 8th, 11th, and 15th days in the hospital. Since culture and PCR results continued to be negative following the change in antibiotic regimen, the externalized VPS was removed and a new temporary external ventricular drain (EVD) was inserted on her 18th day in the hospital. Antibiotics were continued after the operation. Cultures and PCRs on CSF samples repeated every few days (on the patient's 22nd, 25th, 29th, 33rd, and 37th days in the hospital) consistently showed negative results. On the patient's 38th day in the hospital, a new VPS was inserted and the temporary EVD was removed. Antibiotic treatment was continued for an additional week following insertion of the new VPS. Subsequently, the patient had an uncomplicated postoperative course. CSF cultures and PCR assays for *M. hominis* at the time of the final surgical intervention were both negative. The minimum inhibitory concentration (MIC) values for the isolated *M. hominis*, measured by the microdilution method, were $< 0.12 \mu\text{g/ml}$ and $< 0.06 \mu\text{g/ml}$ for clindamycin and ciprofloxacin, respectively. Each serum and CSF sample was obtained almost 2 hours before the administration of ciprofloxacin and 4 hours before the administration of clindamycin. At all times, the concentrations of the 2 drugs in the serum and the CSF samples were above the MIC of the isolated

M. hominis. The concentrations of these drugs in the CSF samples are shown in Fig. 3. The patient was discharged, fully recovered, on her 50th day of hospitalization. At 1 year after the VPS reinsertion, the patient was healthy, without sequelae, and with no evidence of any infection recurrence.

Discussion

Infections are known to occur following VPS insertion in approximately 3%–20% of patients (about 3% in our institute in the past 3 years), and these infections can occur either with or without CNS involvement.^{14,15} *M. hominis* has been rarely reported as a causative agent for VPS infection in the past and the appropriate treatment for such infection remains unclear. The only previously reported symptomatic case of VPS infection caused by *M. hominis* was an 11-year-old girl with hydrocephalus.¹⁰ In this case, the shunt became infected just 3 weeks after insertion and *M. hominis* was cultured from the patient's CSF, which also showed pleocytosis. This patient was first treated with vancomycin plus erythromycin. Although in this case the patient's symptoms and CSF findings were initially relieved, the infection recurred following treatment. The patient was then administered methacycline and the VPS was removed. Unfortunately, the patient died during this therapy.

Some cases have also been reported of *M. hominis* infection with CNS involvement following neurosurgical procedures. Whitson et al.²¹ reported 11 postoperative cases of *M. hominis* CNS infections following neurosurgical intervention. All patients except an 11-year-old girl

FIG. 3. Ciprofloxacin (CPFX) and clindamycin (CLDM) concentrations in the patient's CSF. The determined concentrations of the 2 drugs remained consistently above the MIC of the isolated *M. hominis* at all times (dashed line shows the MIC of clindamycin and dashed-and-dotted line shows the MIC of ciprofloxacin). In addition, the concentration of each drug in the serum remained consistently above the MIC at all times. Figure is available in color online only.

with scoliosis were adults. None of these patients underwent a VPS insertion procedure. Although inappropriate therapies were administered and washout surgeries were required for some of these patients, most of the patients were treated with tetracyclines and/or fluoroquinolones and after diagnosis they had good outcomes.

In our case, the VPS infection with CNS involvement was successfully treated with intravenous clindamycin plus ciprofloxacin therapy in addition to VPS externalization, EVD revision, and subsequent VPS replacement. Although *M. hominis* is not generally susceptible to antibiotics used for pediatric infections, previously reported cases have demonstrated that the optimal antibiotic agents against *M. hominis* include chloramphenicol, clindamycin, quinolones, and tetracyclines.⁴ Although tetracyclines can achieve good CSF penetration, their undesirable adverse effects on teeth and bones in children have led to a general hesitation when it comes to their application. Chloramphenicol has also been associated with the risk of irreversible aplastic anemia. For these reasons, quinolones and clindamycin appeared to be good options and we thus treated our current patient with both of these drugs. Ciprofloxacin, which we administered to the patient as a quinolone agent, has also been reported to be associated with the risk of adverse musculoskeletal events, but these events are reversible.¹

In our therapy of the patient with clindamycin and ciprofloxacin, monitoring of the concentrations of the 2 drugs in the patient's serum and CSF and repeated PCR of *M. hominis* in her CSF were also performed, for the following reasons: 1) parenteral moxifloxacin, which has been shown to be more effective against *M. hominis* infections among the quinolones,² is not available in Japan; 2) clindamycin is known for its poor CSF penetration; and 3) there has been no report of a successfully treated case with VPS infection caused by *M. hominis* in the past, so no data were available to support the use of these drugs to treat this type of infection. We also used the microdilution method to determine the MIC values of the 2 drugs for the *M. hominis* isolated from cultures and verified that the concentrations of both drugs consistently remained above these MIC values. The results suggested that the ciprofloxacin and clindamycin were effective in our case.

The patient required 58 days of hospitalization, which seemed to be a long period of inpatient care for a VPS infection. According to previously reported cases, treatment durations of *M. hominis* extragenital infections vary widely. Because there was no previous report of a successfully treated case with VPS infection, we decided to pursue a 6-week course of parenteral antibiotic administration. The duration of therapy was determined from the 1st day of PCR-negative results of the patient's CSF sample. This 6-week period is one of the longest reported treatment durations; however, because of the lack of data from similar cases, it was difficult to determine the appropriate length of treatment for this infection.

In some reported cases, particularly in neonates, patients have presented with no symptomatic conditions and no treatment has been required despite the isolation of *M. hominis* from their CSF.^{16–19} However, in many cases patients have died or suffered from permanent neurological

sequelae. Because our experience of *M. hominis* infections in children is very limited, we urgently need to conduct further research to investigate the significance and natural history of these infections. In our case, as well as in previously reported cases, *M. hominis* infection presented an invasive course but was controlled soon after treatment was changed to an effective antibiotic regimen.

Conclusions

As our case highlights, when beta-lactam antibiotics are ineffective against VPS infections, and when Gram staining of clinical specimens is unable to detect the causative pathogens, then it is important to consider *M. hominis* as the atypical pathogen. In addition, our combined treatment with ciprofloxacin plus clindamycin was effective against the VPS infection with little concern for possible adverse effects of these drugs in a pediatric patient.

References

1. Adefurin A, Sammons H, Jacqz-Aigrain E, Choonara I: Ciprofloxacin safety in paediatrics: a systematic review. **Arch Dis Child** 96:874–880, 2011
2. Bébér CM, de Barbeyrac B, Pereyre S, Renaudin H, Clerc M, Bébér C: Activity of moxifloxacin against the urogenital mycoplasmas *Ureaplasma* spp., *Mycoplasma hominis* and *Mycoplasma genitalium* and *Chlamydia trachomatis*. **Clin Microbiol Infect** 14:801–805, 2008
3. Blanchard A, Yáñez A, Dybvig K, Watson HL, Griffiths G, Cassell GH: Evaluation of intraspecies genetic variation within the 16S rRNA gene of *Mycoplasma hominis* and detection by polymerase chain reaction. **J Clin Microbiol** 31:1358–1361, 1993
4. Cherry JD, Quanquin NM: *Mycoplasma hominis*, in Cherry J, Demmler-Harrison G, Kaplan S, et al (eds): **Feigin and Cherry's Textbook of Pediatric Infectious Diseases**, ed 7. Philadelphia: Saunders, 2013, Vol 2, pp 2692–2693
5. Chong JS, Tseung SY, Lam HS, Chu WC, Ip M, Wong HT, et al: Successful treatment of multiple subdural empyemata caused by *Mycoplasma hominis* in a newborn. **Neonatology** 95:179–182, 2009
6. Dan M, Tyrrell DL, Stemke GW, Robertson J: *Mycoplasma hominis* septicemia in a burned infant. **J Pediatr** 99:743–745, 1981
7. Dominguez SR, Littlehorn C, Nyquist AC: *Mycoplasma hominis* endocarditis in a child with a complex congenital heart defect. **Pediatr Infect Dis J** 25:851–852, 2006
8. Hata A, Honda Y, Asada K, Sasaki Y, Kenri T, Hata D: *Mycoplasma hominis* meningitis in a neonate: case report and review. **J Infect** 57:338–343, 2008
9. Hummell DS, Anderson SJ, Wright PF, Cassell GH, Waites KB: Chronic recurrent multifocal osteomyelitis: are mycoplasmas involved? **N Engl J Med** 317:510–511, 1987
10. Madoff S, Hooper DC: Nongenitourinary infections caused by *Mycoplasma hominis* in adults. **Rev Infect Dis** 10:602–613, 1988
11. Meyer RD, Clough W: Extragenital *Mycoplasma hominis* infections in adults: emphasis on immunosuppression. **Clin Infect Dis** 17 (Suppl 1):S243–S249, 1993
12. Neilan BA, Jacobs D, Del Dot T, Blackall LL, Hawkins PR, Cox PT, et al: rRNA sequences and evolutionary relationships among toxic and nontoxic cyanobacteria of the genus *Microcystis*. **Int J Syst Bacteriol** 47:693–697, 1997
13. Pascual A, Perez MH, Jaton K, Hafén G, Di Bernardo S, Cotting J, et al: *Mycoplasma hominis* necrotizing pleuropneu-

- monia in a previously healthy adolescent. **BMC Infect Dis** **10**:335, 2010
14. Prusseit J, Simon M, von der Brelie C, Heep A, Molitor E, Völz S, et al: Epidemiology, prevention and management of ventriculoperitoneal shunt infections in children. **Pediatr Neurosurg** **45**:325–336, 2009
15. Simpkins CJ: Ventriculoperitoneal shunt infections in patients with hydrocephalus. **Pediatr Nurs** **31**:457–462, 2005
16. Valencia GB, Banzon F, Cummings M, McCormack WM, Glass L, Hammerschlag MR: Mycoplasma hominis and Ureaplasma urealyticum in neonates with suspected infection. **Pediatr Infect Dis J** **12**:571–573, 1993
17. Waites KB, Duffy LB, Baldus K, Aronin PA, Cassell GH: Mycoplasmal infections of cerebrospinal fluid in children undergoing neurosurgery for hydrocephalus. **Pediatr Infect Dis J** **10**:952–953, 1991
18. Waites KB, Duffy LB, Crouse DT, Dworsky ME, Strange MJ, Nelson KG, et al: Mycoplasmal infections of cerebrospinal fluid in newborn infants from a community hospital population. **Pediatr Infect Dis J** **9**:241–245, 1990
19. Waites KB, Rudd PT, Crouse DT, Canupp KC, Nelson KG, Ramsey C, et al: Chronic Ureaplasma urealyticum and Mycoplasma hominis infections of central nervous system in preterm infants. **Lancet** **1**:17–21, 1988
20. Watson L, Pang YM, Mitchell S, Dodgson A: Mycoplasma hominis meningitis in a 24 week premature neonate: case report and short literature review. **J Pediatr Pharmacol Ther** **13**:251–254, 2008
21. Whitson WJ, Ball PA, Lollis SS, Balkman JD, Bauer DF: Postoperative Mycoplasma hominis infections after neurosurgical intervention. **J Neurosurg Pediatr** **14**:212–218, 2014
22. Wolthers KC, Kornelisse RF, Platenkamp GJ, Schuurman-Van Der Lem MI, van der Schee C, Hartwig NG, et al: A case of Mycoplasma hominis meningo-encephalitis in a full-term infant: rapid recovery after start of treatment with ciprofloxacin. **Eur J Pediatr** **162**:514–516, 2003

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Sato. Acquisition of data: Sato, Kubota, Katsuyama, Suzuki, Miyairi. Analysis and interpretation of data: Sato, Kubota, Katsuyama. Drafting the article: Sato. Critically revising the article: Kubota, Katsuyama, Suzuki, Minami, Kasai. Reviewed submitted version of manuscript: Miyairi, Minami, Kasai. Approved the final version of the manuscript on behalf of all authors: Sato. Administrative/technical/material support: Kubota, Katsuyama.

Correspondence

Masanori Sato, Department of Pediatric Intensive Care, Nagano Children's Hospital, 3100, Toyoshina, Azumino City, Nagano 399-8288, Japan. email: watasihhasatoanataha@yahoo.co.jp.