Case Report

Fatal nosocomial meningitis caused by *Mycoplasma hominis* in an adult patient: case report and review of the literature

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**SUMMARY**

Meningitis due to *Mycoplasma hominis* in adults is rarely described, with only three cases having been reported to date. A case of fatal meningitis in a 39-year-old patient after a neurosurgical procedure for a subarachnoid haemorrhage is reported herein. Identification and treatment were significantly delayed because of the rarity of the aetiology and difficulty identifying this organism with the routinely used conventional methods, such as Gram staining and agar growth on standard agar plates. Clinical procedures and the treatment of ‘culture-negative’ central nervous system infections is a real challenge for clinical microbiologists and clinicians, and *M. hominis* has to be considered as a potential, although very uncommon, pathogen.

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1. Introduction

*Mycoplasma hominis* is a well-known bacterium colonizing the genito-urinary tract, especially in sexually active adolescent females. Extragenital infections are rare. To date, only 16 cases of central nervous system (CNS) infection caused by *M. hominis* have been described since 1950 (Table 1). A new case of meningitis caused by this bacterium in an adult, following a neurosurgical procedure, is reported here.

2. Case report

A 39-year-old man with a history of untreated hypertension, chronic alcoholism, and active smoking was admitted to the emergency department after a loss of consciousness linked to a history of a fall. Injuries included a subarachnoid haemorrhage (Fisher grade III) due to a ruptured pericallosal left artery aneurism, which was embolized when diagnosed. An external ventricular drain (EVD) was placed and suprapubic catheterization was also performed. On transfer to the intensive care unit (ICU), the patient was initially febrile. Neurological and respiratory failure occurred 1 week later (day 8) and the patient required tracheal intubation. Antibiotherapy consisting of piperacillin–tazobactam plus linezolid was given for 3 days, and this was then switched to ceftriaxone plus linezolid due to a suspicion of nosocomial pneumonia. The pneumonia was confirmed by culture of the Combicath, which harboured 10⁶ CFU/ml Streptococcus pneumoniae. Computed tomography (CT) perfusion imaging revealed a peri-aureysmal haematomy and spasms of the anterior cerebral arteries (ACA) and right middle cerebral artery (MCA), without surgical indication. Arteriography confirmed a severe vasospasm of the bilateral ACA an MCA, and endovascular therapy with milrinone and nimodipine was started.

Between days 8 and 12, several febrile episodes occurred despite the antibiotics prescribed for the suspected pneumonia. Multiple cerebrospinal fluid (CSF) samples (days 8, 10, 11, and 12) were analyzed and returned sterile. A cell count was not performed because of the haemorrhagic nature of the samples; direct examination was also negative. On day 13, in view of this presentation of aseptic meningitis, the patient was started on

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treatment with meropenem plus vancomycin for 14 days and the EVD was changed. Analysis of the CSF samples collected on days 16, 17, and 20 showed a decrease in the leukocyte count (2.3, 0.53, and 0.33 × 10³/L, respectively) and all bacterial cultures of CSF samples remained sterile.

Follow-up imaging on day 21 showed moderate hydrocephaly with ischemic areas in both territories of the ACA. Sedation of the patient was then ended, and a neurological evaluation revealed tetraparesis and varying responses to simple orders. A new EVD was placed on day 22 to manage the hydrocephaly. CSF collected during the procedure was still abnormal (0.74 × 10³ leukocytes/L with 94% neutrophils). At the same time, serological testing for HIV, hepatitis C virus, and hepatitis B virus was done; all tests were negative. Cytomegalovirus (CMV) serology in the CSF was positive for IgG and IgM suggesting reactivation in the CSF. Mycological cultures were all negative, including those for Cryptococcus. PCR of CSF samples for mycobacterial infections, Mycoplasma pneumoniae, Chlamydia pneumoniae, CMV, herpes simplex virus, varicella zoster virus, and enterovirus were also negative. Nevertheless, due to the presence of tiny microcolonies on blood agar plates, 16S rRNA gene sequencing was performed directly from the colonies. The CSF sample obtained on day 33 was positive for Mycoplasma hominis by quantitative real-time PCR (qPCR) [10].

Selective agar for M. hominis (A7 Mycoplasma; bioMérieux, Marcy l’Etoile, France) was used to culture a CSF sample and was positive, showing the typical ‘fried egg’ colonies. An antibiogram performed using a Mycofast Revolution kit (Elitech, Puteaux, France) revealed sensitivity to clindamycin, tetracycline, levofloxacin, and moxifloxacin and confirmed intrinsic resistance to erythromycin. All CSF samples from day 22 to day 34 were recovered and cultured on specific agar plates for Mycoplasma spp. All of these specimens were positive for M. hominis. Interestingly, identification by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) was not possible, even after acetonitrile extraction.

Once the diagnosis had been made, moxifloxacin was added to the other antibiotics from day 34 to day 49. Three days after introducing the treatment, the patient’s neurological status declined. Magnetic resonance imaging (MRI) performed the day after showed cortical laminar necrosis associated with tetraventricular hydrocephaly. Due to the lack of improvement, the patient’s critical condition, and the severe irreversible lesions, the ethics staff decided to limit further therapeutic procedures and the patient died on day 80.

3. Discussion

M. hominis is found in the human urogenital tract with a prevalence of approximately 15% and is mainly involved in urogenital infections and neonatal infections. Nevertheless, the pathogenicity of this species may be difficult to assess because it is often present as a commensal organism. Although rare, extra-genital infections have been described, such as bone and joint infections and CNS infections, especially in newborn infants and immunocompromised patients. In adults, only 16 cases of CNS infection have been described since 1950, with 13 cases of brain abscesses and three cases of meningitis (two postoperative infections and one secondary to septic arthritis) [11-13,15] (Table 1). In all cases described, the patients presented contributing factors such as a head trauma, neurosurgery, or genitourinary or delivery manipulations. In the case presented here, the patient suffered a subarachnoid haemorrhage and had a urinary catheter, two important comorbidities for CNS infections caused by M. hominis.

The lack of bacterial cell wall components makes M. hominis undetectable by Gram staining. Bacterial culture is very slow (2–5 days) and requires specific agar plates enriched with arginine. On appropriate media, M. hominis produces typical fried egg shaped colonies. Culture is the gold standard procedure for identification, nevertheless only a few microbiology laboratories have used specific agar for M. hominis in meningitis cases. Blood culture systems appear to be ineffective for the detection of M. hominis. Studies have reported identification using MALDI-TOF MS [13] and molecular techniques such as 16S rRNA gene sequencing and real-time PCR [11,15]. In the case reported here, identification of M. hominis was performed using TaqMan quantitative real-time

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)/sex</th>
<th>Sample</th>
<th>Diagnosis</th>
<th>Diagnosis technique(s)</th>
<th>Author, year</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20/M</td>
<td>Abscess</td>
<td>PT brain abscess</td>
<td>Culture</td>
<td>Paine et al., 1950</td>
</tr>
<tr>
<td>2</td>
<td>29/M</td>
<td>Abscess</td>
<td>PO brain abscess</td>
<td>Culture</td>
<td>Payan et al., 1981</td>
</tr>
<tr>
<td>3</td>
<td>76/M</td>
<td>CSF</td>
<td>PO meningitis</td>
<td>Culture</td>
<td>McMahon et al., 1990</td>
</tr>
<tr>
<td>4</td>
<td>18/F</td>
<td>CSF</td>
<td>PO meningitis</td>
<td>Culture</td>
<td>Cohen and Kubak, 1997</td>
</tr>
<tr>
<td>5</td>
<td>22/F</td>
<td>Abscess</td>
<td>PO brain abscess</td>
<td>ELISA</td>
<td>Zheng et al., 1997</td>
</tr>
<tr>
<td>6</td>
<td>40/F</td>
<td>Abscess</td>
<td>Brain abscess</td>
<td>16S rDNA</td>
<td>House et al., 2003</td>
</tr>
<tr>
<td>7</td>
<td>17/F</td>
<td>CSF, blood</td>
<td>PP brain abscess</td>
<td>Culture</td>
<td>Douglas et al., 2003</td>
</tr>
<tr>
<td>8</td>
<td>40/M</td>
<td>Abscess</td>
<td>PT brain abscess</td>
<td>16S rDNA</td>
<td>Kupila et al., 2006</td>
</tr>
<tr>
<td>9</td>
<td>48/M</td>
<td>CSF, bone graft</td>
<td>PO brain abscess</td>
<td>16S rDNA</td>
<td>McCarthy and Looke, 2008</td>
</tr>
<tr>
<td>10</td>
<td>17/F</td>
<td>Abscess, soft tissues</td>
<td>PO brain abscess</td>
<td>Culture</td>
<td>McCarthy and Looke, 2008</td>
</tr>
<tr>
<td>11</td>
<td>41/F</td>
<td>Abscess</td>
<td>Post abortion brain abscess</td>
<td>16S rRNA</td>
<td>Al Masalma et al., 2011</td>
</tr>
<tr>
<td>12</td>
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<td>CSF</td>
<td>PO brain abscess</td>
<td>16S rRNA</td>
<td>Lee et al., 2012</td>
</tr>
<tr>
<td>13</td>
<td>26/M</td>
<td>CSF</td>
<td>Meningitis (secondary to SA)</td>
<td>16S rDNA</td>
<td>Sato et al., 2012</td>
</tr>
<tr>
<td>14</td>
<td>40/M</td>
<td>Abscess</td>
<td>PT brain abscess</td>
<td>16S rDNA</td>
<td>Henao-Martínez et al., 2012</td>
</tr>
<tr>
<td>15</td>
<td>43/M</td>
<td>Intracranial pressure sensor</td>
<td>Subdural hematoma</td>
<td>Culture</td>
<td>Pailhoriés et al., 2014</td>
</tr>
<tr>
<td>16</td>
<td>21/F</td>
<td>Biopsy</td>
<td>Spinal abscess after peridural procedure</td>
<td>MALDI-TOF MS</td>
<td>16S rDNA</td>
</tr>
<tr>
<td>17</td>
<td>39/M</td>
<td>CSF</td>
<td>PO meningitis</td>
<td>Specific qPCR</td>
<td>This case, 2016</td>
</tr>
</tbody>
</table>

CSF, cerebrospinal fluid; CNS, central nervous system; F, female; M, male; MALDI-TOF MS, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry; PO, postoperative; PP, post-partum; PT, post-traumatic; SA, septic arthritis.
PCR and specific agar culture. Interestingly, MALDI-TOF MS (Microflex; Bruker, Bremen, Germany) failed to identify \textit{M. hominis}. It is assumed that growth on blood agar plates does not allow identification, because all previous cases that were identified by MALDI-TOF MS reported growth on specific agar, such as PPLO medium and Hayflick arginine medium.\textsuperscript{14} Moreover, \textit{M. hominis} spectra used for MALDI-TOF identification were not available in the initial Bruker software library.

\textit{M. hominis} is intrinsically resistant to a variety of antibiotic classes such as \beta-lactams, glycopeptides, fosfomycin, sulfonamides, and macrolides. The major antibiotics active against \textit{M. hominis} are the tetracyclines, lincosamides, chloramphenicol, and fluoroquinolones. In the case presented here, an antibiogram was performed and revealed susceptibility to clindamycin, tetracycline, levofloxacin, and moxifloxacin. As \textit{M. hominis} CNS infections may result in aseptic lymphocytic meningitis syndrome, which is treated empirically with antibiotics active on the bacterial cell wall such as third-generation cephalosporins, the change to appropriate targeted therapeutic management could be delayed significantly. In this case, the patient received appropriate antibiotic therapy 24 days after the onset of symptoms. Fluoroquinolones (e.g., moxifloxacin and levofloxacin) have been described as providing effective therapy with significant CNS penetration,\textsuperscript{9,11} and the side effects are less significant compared to those of other effective therapeutics such as chloramphenicol or cyclins.

In conclusion, this case of \textit{M. hominis} meningitis shows that empirical antibiotic treatment for nosocomial aseptic meningitis has a high chance of failure and that the new technique of real-time PCR appears to be more effective and faster than routine bacterial culture. Despite the death of this patient, moxifloxacin could be considered effective against \textit{M. hominis}, as has been described previously in other studies. \textit{M. hominis} should be considered as a causative agent of CNS infection after neurosurgical procedures, especially if there is no rapid response to antimicrobial therapy and routine culture of CSF samples remains negative.

\textbf{Conflict of interest:} The authors declare that they have no conflict of interest.

\textbf{References}