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CASE REPORT

Mycoplasma hominis meningitis after operative neurosurgery: A case report and review of literature

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Abstract

BACKGROUND

Mycoplasma hominis (*M. hominis*), which causes central nervous system infections in adults, is very rare. It is also relatively difficult to culture mycoplasma and culturing requires special media, resulting in a high rate of clinical underdiagnosis. Therefore, clinicians often treat patients based on their own experience before obtaining pathogenic results and may ignore infections with atypical pathogens, thus delaying the diagnosis and treatment of patients and increasing the length of hospital stay and costs.

CASE SUMMARY

A 44-year-old man presented to the hospital complaining of recurrent dizziness for 1 year, which had worsened in the last week. After admission, brain magnetic resonance imaging (MRI) revealed a 7.0 cm × 6.0 cm × 6.1 cm lesion at the skull base, which was irregular in shape and had a midline shift to the left. Based on imaging findings, meningioma was our primary consideration. After lesion resection, the patient had persistent fever and a diagnosis of suppurative meningitis based on cerebrospinal fluid (CSF) examination. The patient was treated with the highest level of antibiotics (meropenem and linezolid), but the response was ineffective. Finally, *M. hominis* was detected by next-generation metagenomic sequencing (mNGS) in the CSF. Therefore, we changed the antibiotics to moxifloxacin 0.4 g daily combined with doxycycline 0.1 g twice a day for 2 wk, and the patient had a normal temperature the next day.

CONCLUSION

Mycoplasma meningitis after neurosurgery is rare. We can use mNGS to detect *M. hominis* in the CSF and then provide targeted treatment.

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Core Tip: Mycoplasma meningitis after neurosurgery is relatively rare. Intracranial infections with atypical pathogens are difficult to identify. Because *Mycoplasma hominis* (*M. hominis*) has no cell wall, it cannot be observed by Gram staining. Moreover, the difficulty of culturing *M. hominis* increases the challenge of clinical detection and often delays treatment. Next-generation metagenomic sequencing can be used to identify the pathogen in the early stage of the disease.

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INTRODUCTION

Mycoplasma hominis (*M. hominis*) is a common colonizer in the microflora of the genitourinary tract of many sexually active adolescent females. *M. hominis* can be found in the cervical or vaginal secretions of up to 50% of healthy women[1]. At present, it has been demonstrated that pathogenic *M. hominis* is mainly distributed in the oropharynx and urogenital tract[2]. *M. hominis* is associated with certain diseases of parturient women, their fetuses and newborns, but it is rare for *M. hominis* to cause central nervous system infections in adults. Because *M. hominis* has no cell wall, it cannot be observed by Gram staining. Moreover, the difficulty of culturing *M. hominis* increases the challenge of clinical detection and often delays treatment. Here, we report a case of *M. hominis* infection secondary to craniocerebral surgery detected by next-generation metagenomic sequencing (mNGS). We also reviewed relevant literature to analyze the clinical features, diagnosis and treatment methods of central nervous system infections caused by *M. hominis* to deepen the understanding of this type of infection among clinicians and improve the diagnosis and treatment options.

CASE PRESENTATION

Chief complaints

A 44-year-old man presented to our hospital complaining of worsening dizziness.

History of present illness

One year before admission, the patient suffered from repeated episodes of dizziness without blurred vision, nausea, vomiting or limb dysfunction. However, the symptom did not cause alarm. A week ago, his dizziness worsened, and he presented to the hospital.

History of past illness

Healthy, with no specific diseases.

Physical examination

Physical examination upon admission showed that the patient had no nystagmus, no neck rigidity, normal muscle strength and muscular tension of the limbs, and negative pathological signs.

Laboratory examinations

On admission, the patient's examination results were completely normal, including

leukocyte count, hypersensitive C-reactive protein, procalcitonin, electrolytes, liver and kidney function tests and coagulation function tests. On the third postoperative day, the leukocyte count was 14.8 × 10^9/L (reference range: 4-10 × 10^9/L), and the neutrophil count (NEUT%) was 89.5% (reference range: 40%-75%). The cerebrospinal fluid (CSF) examination showed 62.9 × 10^3 white blood cell (WBC)/μL, with a protein level of 8036 mg/L, glucose level of 3.8 mmol/L and chloride ion concentration of 139 mmol/L.

Imaging examinations

The brain magnetic resonance imaging (MRI) examination revealed a massive mass outside the right anterior and middle cranial base. The main body of the lesion was in the middle cranial base with an irregular shape and a size of approximately 7.0 cm × 6.0 cm × 6.1 cm. The right ventricle and cerebral peduncle were compressed, and the midline was shifted to the left (Figure 1). On postoperative day 10, we reviewed the brain MRI and excluded a brain abscess (Figure 2).

FINAL DIAGNOSIS

The initial diagnosis on admission was intracranial space-occupying meningioma. Meningioma, *M. hominis* meningitis and pulmonary infection were diagnosed postoperatively.

TREATMENT

The patient was admitted to the hospital, and preoperative examinations were completed. The patient underwent intracranial tumor resection on May 4, 2020. The operation lasted approximately 9 h, and the intraoperative bleeding volume was 2000 mL. Preoperative and postoperative cefathiamidine was used to prevent infection. On the second day after surgery, the patient was conscious. The muscle strength of the left limb was approximately grade 3, whereas the muscle strength of the right limb was normal. The patient was extubated successfully on postoperative day 3. Also, on postoperative day 3, the patient developed fever with a temperature of 38.3°C. Laboratory studies revealed that the leukocyte count was 14.8 × 10^9/L (reference range: 4-10 × 10^9/L), and the NEUT% was 89.5% (reference range: 40%-75%). Then, we changed the antibiotic to cefoperazone-sulbactam. However, the patient's temperature continued to increase. At this time, we found that the patient had neck rigidity. Thus, we performed a lumbar puncture. The CSF examination showed a WBC level of 62.9 × 10^3 WBC/μL, protein level of 8036 mg/L, glucose level of 3.8 mmol/L and chloride ion concentration of 139 mmol/L. Blood cultures drawn on postoperative day 3 revealed *Staphylococcus* infection. The antibiotics were changed to meropenem and norvancomycin on postoperative day 6, and a brain abscess was excluded by brain MRI (Figure 2). *M. hominis* was detected in the CSF by mNGS on postoperative day 12. At that time, we believed that *M. hominis* meningitis was rare, the possibility of mycoplasma intracranial infection was low, and the possibility of contamination was high. Thus, we did not adjust the treatment plan. Afterwards, the patient was treated with linezolid and levofloxacin successively, but the body temperature still fluctuated between 38 °C and 39 °C. Just when we were at a loss, we discussed and developed a treatment plan with the neurosurgeons, infectious disease specialists, and hematologists and decided to use special media to culture the CSF for mycoplasma. We also reviewed the literature on *M. hominis* meningitis. A total of 19 studies published from inception to the end of June 2020 were retrieved, including 11 cases of *M. hominis* brain abscess, 6 cases of meningitis and 2 cases of spinal cord abscess (Table 1). Finally, *M. hominis* was cultured from the CSF, which confirmed the mNGS results. We finally changed the antibiotic to moxifloxacin combined with doxycycline on postoperative day 18. The patient's temperature returned to normal on the second day after adjustment of the treatment plan, and the patient was later discharged from the hospital (Figure 3).

OUTCOME AND FOLLOW-UP

At follow-up 1 year later, the muscle strength of the patient's left limb had returned to

Table 1 A review of the literature on intracranial infection with *Mycoplasma hominis* in adults

Ref.	Year published	Country	Sex	Age (yr)	History	Preoperative diagnosis	Risk factors	Clinical symptoms	DM	Specimens	IM	Antibiotics used after diagnosis	Outcomes
Paine *et al* [15]	1950	USA	M	20	No	Eyeball trauma	Head trauma	Fever, headache, neck stiffness	C	P	BA	St	Cure
Payan *et al* [16]	1981	USA	M	29	No	Subdural hematoma, brain contusion	Motor vehicle accident	Fever, disturbance of consciousness	C	P	BA	Te+Er	Cure
McMahon *et al*[17]	1990	USA	M	76	Hypertension	Subarachnoid hemorrhage	Urethral catheterization	Fever, disturbance of consciousness	C	CSF	Meningitis	-	Death
Kersten *et al*[18]	1995	USA	M	20	No	Eye contusion, hematoma of frontotemporal lobe	Motor vehicle accident, head trauma, hormone therapy	Fever, right eye swelling	C	P	Right eye abscess, BA	Dox + Cli	Cure
Zheng *et al* [19]	1997	USA	F	22	No	Right frontal lobe cerebral hemorrhage	Vaginal delivery	Fever, left-sided weakness	ELISA	P	BA	-	Cure
Cohen *et al* [20]	1997	USA	F	18	No	Subdural hemorrhage, ventricular hemorrhage	Motor vehicle accident	Fever	C	CSF	Meningitis	Dox + Cip + Ery	Cure
House *et al* [21]	2003	USA	F	40	No	Cavernous hemangioma of the right frontal lobe	Perineal ulcers	Fever, nausea, limb dysfunction	C + NGS	P	BA	Cip + Met	Cure
Kupila *et al* [7]	2006	Finland	M	40	No	Scalp laceration	Head trauma, cystoscopy, catheterization	Disturbance of consciousness	NGS	P	BA	Te	Cure
McCarthy *et al*[22]	2008	Australia	M	48	No	Intracranial colloid cyst	Surgical infection	Fever, disturbance of consciousness	NGS + C	Subdural empyema, bone flap	BA	Gat	Cure
Al Masalma *et al*[23]	2011	USA	F	41	No	Spontaneous abortion	Dilatation and curettage	Disturbance of consciousness	NGS	P	BA	Dox	Cure
Lee *et al*[24]	2012	Netherlands	F	48	No	Subarachnoid hemorrhage	Ventricular drainage tube	Fever	NGS + C	CSF	Meningitis	Mox	Cure
Sato *et al* [25]	2012	Japan	M	26	Hypogammaglobulinemia	Arthritis	Hypogammaglobulinemia	Joint swelling and pain, headache	C+NGS	CSF, joint effusion, blood	Meningitis	-	Death
Henao-Martínez *et al*[26]	2012	USA	M	40	No	Right subdural hematoma, subarachnoid	Head trauma	Fever	C+NGS	Brain debridement tissue	BA	Dox	Cure

						hemorrhage, cerebral contusion							
Pailhoriès *et al*[27]	2014	France	M	43	Chronic alcoholism, TIA, epilepsy	Subdural hematoma, left frontal hematoma	Head trauma, urethral catheterization	Fever	MALDI-TOF MS□NGS	Electrodes, P	BA	Lev + Dox	Cure
Hos *et al* [28]	2015	Germany	F	21	No	Spinal abscess	Vaginal delivery, epidural blood tape therapy	Fever, neck pain, vomiting	NGS+C	CSF	SA	Mox	Cure
Zhou *et al* [29]	2016	China	M	79	Hypertension	Cerebral hemorrhage	Urethral catheterization	Fever, disturbance of consciousness, right-sided weakness	NGS	CSF	Meningitis	Azi + Dox + Min	Cure
Reissier *et al*[30]	2016	France	M	39	Hypertension, chronic alcoholism	Subarachnoid hemorrhage	Cystostomy	Disturbance of consciousness, fever	C, real-time PCR	CSF	Meningitis, hydrocephalus	Mox	Death
Parsonson *et al*[31]	2016	Australia	F	30	Polycystic ovary syndrome, depression, obesity	Lumbar disc herniation	Repeated operations	Festering wounds	NGS	P	SA	Mox	Cure
Bergin *et al* [32]	2017	Singapore	M	57	No	Arteriovenous malformation with hemorrhage	Urethral catheterization	Fever	NGS	Surgical specimens	BA	Dox	Cure

DM: Diagnosis method; IM: Infection manifestations; St: Streptomycin; Te: Tetracycline; Er: Erythromycin; Dox: Doxycycline; Cli: Clindamycin; Cip: Ciprofloxacin; Ery: Erythromycin; Met: Metronidazole; Gat: Gatifloxacin; Lev: Levofloxacin; Mox: Moxifloxacin; Azi: Azithromycin; Min: Minocycline; C: Culture; P: Pus; CSF: Cerebrospinal fluid; BA: Brain abscess; SA: Spinal abscess.

normal, and the patient could work normally.

DISCUSSION

Intracranial infection is a common complication after neurosurgery with a reported incidence of less than 10% and a high incidence at 3 to 7 d postoperatively. Infection is mainly caused by Gram-positive bacteria, which can manifest as subdural empyema, brain abscess, ventriculitis, or meningoencephalitis[3,4]. In recent years, the epidemiology of pathogenic bacteria causing intracranial infections after neurosurgery has changed. Gram-negative bacteria exhibit an obvious increasing trend, and multidrug-resistant or extensively drug-resistant *Acinetobacter baumannii* also exhibits a gradually increasing trend[5]. Intracranial infection with *M. hominis* is common in neonates but rare in adults after craniocerebral surgery. Current studies have found that cerebrospinal fluid leakage, ventricular drainage, multiple operations, surgical incision infection, and long operation time (greater than 4 h) are independent risk factors for intracranial infection after craniocerebral surgery[6]. There are three main sources of intracranial infection with mycoplasma: direct contamination during

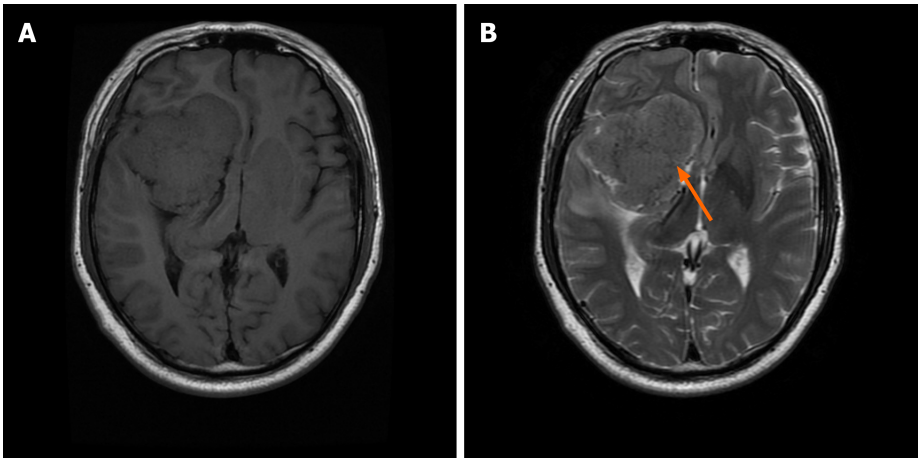

Figure 1 Magnetic resonance imaging scan of the brain. T1- (A) and T2-weighted images (B) showed a large extracerebral mass at the right anterior, middle and posterior cranial base (orange arrow).

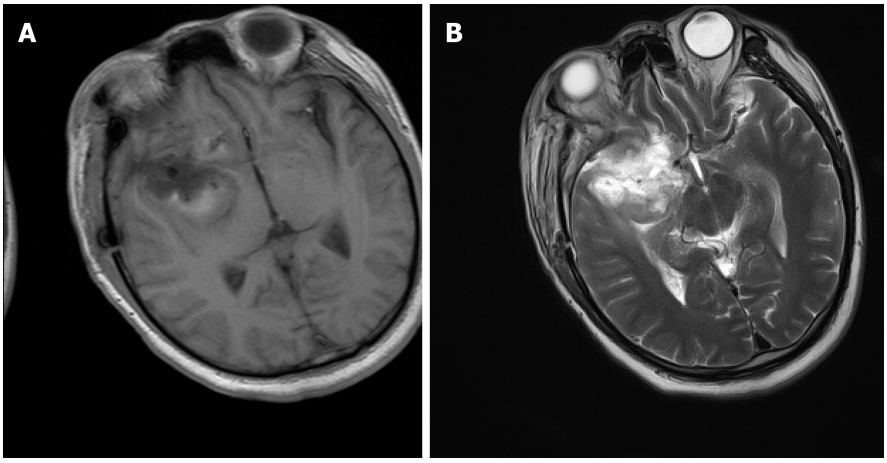

Figure 2 Magnetic resonance imaging scan of the brain on postoperative day 10. T1- (A) and T2-weighted imaging (B) did not reveal an abscess in the surgical area.

trauma, direct contamination during surgery, or bacteremia caused by urogenital tract manipulation secondary to brain site infection. Mycoplasma contains surface proteins that promote cell adhesion and can spread to other sites, leading to infection when the mucosa is damaged, such as with instrument manipulation, surgery, and trauma[1]. Although the results of urine culture were negative many times in this patient, the urinary catheter was continuously indwelling after surgery. Because the urinary tract is a common site of mycoplasma, the possibility of intracranial infection caused by the urinary tract could not be excluded in this patient. Earlier, Kupila *et al*[7] reported a case of brain abscess with *M. hominis* secondary to cystoscopy and an indwelling catheter. In this case, the risk of secondary intracranial infection after surgery was significantly increased due to the large tumor volume, long operation time, greater volume of intraoperative bleeding, and presence of a postoperative extradural drainage tube. The patient developed fever on postoperative day 3, and *Staphylococcus* was detected in blood cultures. Early empirical coverage of Gram-positive bacteria was performed, but the treatment was ineffective. During treatment, we reviewed the relevant domestic and international literature. There have been a few reports on *M. hominis* infection in adults after craniocerebral surgery. In addition, we lacked clinical experience, so the treatment for *M. hominis* was delayed. Fortunately, the patient was finally cured and discharged.

At present, mycoplasma culture is the main method for detection of mycoplasma in domestic medical institutions, and this process mainly uses liquid medium for direct culture with simultaneous drug sensitivity tests. Mycoplasma releases ammonia gas by decomposing arginine, resulting in pH changes in the liquid medium and thus a change in the color of the indicator to infer the culture result. Because cholesterol is an

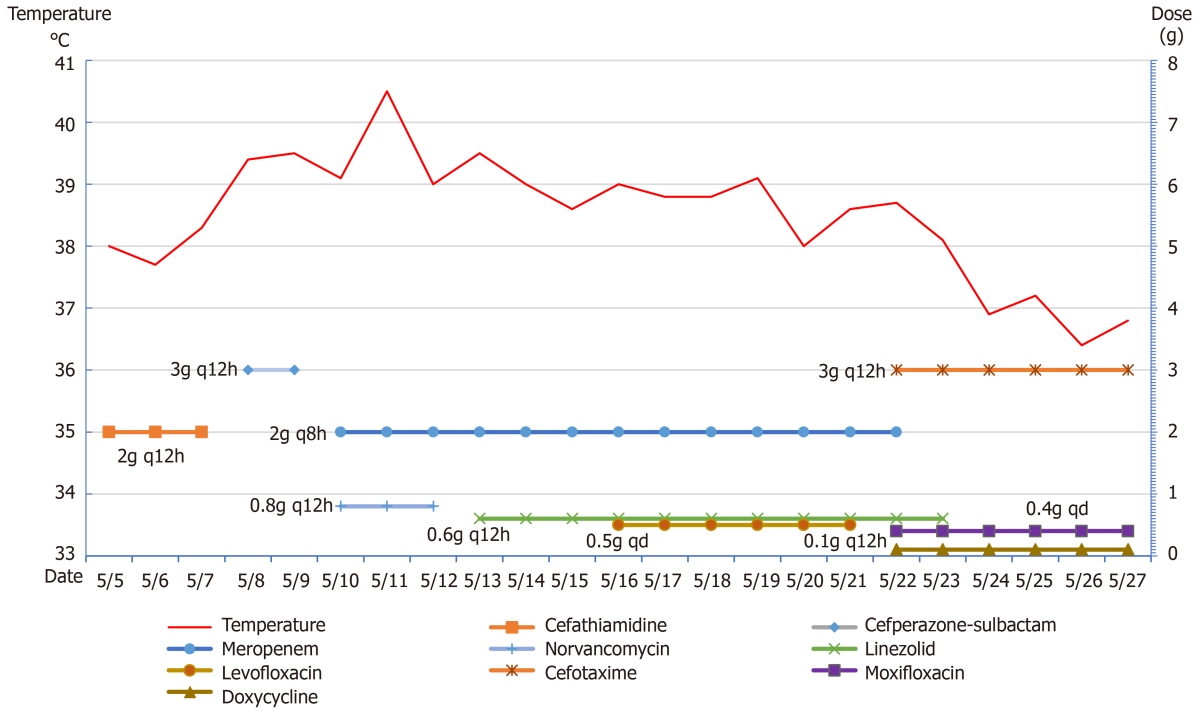

Figure 3 Changes in body temperature and antibiotic use.

important component of the cell membrane of mycoplasma and mycoplasma itself does not have the ability to synthesize it, animal serum must be added to the culture medium *in vitro* to provide cholesterol components. Therefore, the liquid medium must contain arginine and cholesterol. If the solid culture method is adopted, the specimen is cultured in a CO_2 environment for 24-48 h after inoculation and characteristic "fried egg-like" colonies can be observed under the microscope. Due to the uncertainty of the factors leading to pH changes in liquid media, false-positive results may occur. Therefore, the liquid culture method can be combined with the solid culture method in clinical practice to improve the mycoplasma detection rate. The possibility of mycoplasma infection was not considered during the culture of the CSF specimen of this patient, and no special medium was used. Thus, the results of repeated culture were negative. After the mNGS test results suggested *M. hominis*, we cultured the CSF again using special medium, and the results confirmed the intracranial infection caused by *M. hominis*. Most of the cases we reviewed were diagnosed by mNGS, which not only directly sequences the genomes of samples but also identifies a variety of unknown pathogens in the samples. Compared with traditional culture methods, mNGS requires less time and is more efficient[8]. Long *et al*[9] showed that, compared with blood cultures, mNGS had a higher sensitivity and pathogen detection rate (30.77% *vs* 12.82%). Currently, the conserved region of 16S rRNA is the main gene sequence used for the construction of primers. Studies have found that the application of 16S rRNA by real-time reverse transcription PCR (qRT-PCR) can further improve the positive rate of specimen detection and eliminate false-positives[10].

Because mycoplasmas lack a cell wall, they are resistant to β-lactam and glycopeptide antibiotics that act on the cell wall. Tetracyclines that interfere with protein synthesis are commonly used to treat mycoplasmas, which are also sensitive to quinolones that inhibit DNA replication. *M. hominis* is typically resistant to macrolides and aminoglycosides. In the cases reviewed, 9 patients were switched to tetracycline antibiotics after the pathogen was confirmed as *M. hominis*, and all the patients were cured. In patients with meningitis caused by *M. hominis*, if doxycycline treatment fails, clindamycin or fluoroquinolones may be used instead[11]. In the treatment of this patient, levofloxacin was used in the early stages, but the treatment effect was not ideal. After the combined application of moxifloxacin and doxycycline, the patient's body temperature and infection indices gradually improved. *M. hominis* was most sensitive to doxycycline and minocycline but more resistant to erythromycin, norfloxacin and clarithromycin[12]. Although some studies have shown that the drug resistance rate of levofloxacin to mycoplasma has exhibited a declining trend in recent

years, the drug resistance rate of *M. hominis* is approximately 23.08%[13]. However, Zhang *et al*[14] used PCR to amplify drug-resistant genes and found that the drug resistance rate of *M. hominis* to levofloxacin reached 87.9% due to *ParC S911* and *ParC K144R* gene variation. Therefore, doxycycline remains the drug of choice for the treatment of *M. hominis*.

CONCLUSION

M. hominis infection after craniocerebral surgery in adults is rare, but it can be clearly diagnosed by special culture or mNGS. The clinical prognosis is generally good when treated with targeted anti-infection therapy.

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