Neurology Asia 2026; 31(2) : 803 – 809

CASE REPORTS

Mycoplasma hominis central nervous system infection diagnosed by metagenomic next-generation sequencing: A case report

*[1]Shaoqi Wu, *[2]Kangzuo Luo, [3]Jiajun He, [3]Wenfeng Xu, [3]Lifu Diao, [1]Jun Yin
*SQ Wu and KZ Luo contributed equally to this work and are co-first authors

[1]Department of Pharmacy, The Affiliated Shunde Hospital of Jinan University, Foshan, Guangdong, China; [2]Department of Neurosurgery, The Affiliated Shunde Hospital of Jinan University, Foshan, Guangdong, China; [3]Department of Critical Care Medicine (ICU), The Affiliated Shunde Hospital of Jinan University, Foshan, Guangdong, China

Abstract

Mycoplasma hominis (*M. hominis*) is a rare cause of intracranial infection with diagnostic challenges due to its fastidious nature, nonspecific symptoms mimicking common nervous system infection (e.g., viral encephalitis), and absence of characteristic neuroimaging. Traditional methods (culture/serology) often yield false negatives, delaying appropriate therapy. Metagenomic Next-Generation Sequencing (mNGS) provides an unbiased solution for such pathogens. We report a 50-year-old male presented with recurrent fever and coma after hematoma evacuation and external ventricular drainage for cerebral hemorrhage. Empirical antimicrobial therapy (ceftriaxone → piperacillin-tazobactam → vancomycin) was ineffective. Cerebrospinal fluid (CSF) analysis confirmed intracranial infection, leading to escalation to meropenem plus intravenous/intrathecal vancomycin, yet clinical and CSF parameters showed no improvement. Although traditional culture of pathogens and serological testing yielded negative results, *M. hominis* was detected in CSF by mNGS mNGS on postoperative day 19. Targeted therapy with moxifloxacin and doxycycline resulted in marked clinical improvement: fever resolved and CSF abnormalities normalized.

Conclusion: This case highlights mNGS as pivotal for diagnosing fastidious pathogens like *M. hominis* in culture-negative intracranial infections, enabling a critical shift from failed empirical therapy to successful pathogen-directed treatment. It further underscores the indispensable role of the clinical pharmacist in optimizing antimicrobial selection and monitoring based on mNGS findings. When empirical therapy fails and pathogen identification remains elusive in CNS infections, mNGS emerges as a valuable diagnostic option to guide targeted treatment.

Keywords: Mycoplasma hominis, central nervous system infection, metagenomic next-generation sequencing (mNGS), clinical pharmacist, cerebrospinal fluid (CSF)

INTRODUCTION

Post-neurosurgical intracranial infections pose substantial diagnostic challenges, characterized by low culture positivity rates for common pathogens—let alone fastidious or atypical organisms.[1] *M. hominis*, a common pathogen associated with genitourinary tract infections and complications of pregnancy, is rarely reported in central nervous system (CNS) infection.[2] While bacterial pathogens predominate, evidence indicates that organisms like *Mycoplasma* spp.—lacking a cell wall—evade detection by routine methods (Gram stain/culture) and exhibit intrinsic β-lactam resistance, rendering empirical regimens ineffective.[3] Therefore, an effective detection method is lacking to rapidly and accurately detect *M. hominis* infection. Metagenomic next-generation sequencing (mNGS) is considered as a potential rapid

Address correspondence to: Jun Yin, Pharmacy Department, the Affiliated Shunde Hospital of Jinan University, Foshan, Guangdong Province, China. E-mail: yinjun8819@hotmail.com

Date of Submission: 3 December 2025; Date of Acceptance: 9 February 2026

https://doi.org/10.54029/2026sjc

diagnostic method with high sensitivity and specificity for identifying infectious pathogens.[4] We report an adult case after operative neurosurgery where the use of mNGS led to the definitive diagnosis of *Mycoplasma hominis* meningoencephalitis, enabling targeted antimicrobial therapy that resolved a culture-negative, refractory central nervous system (CNS) infection.

CASE REPORT

A 50-year-old male with hypertension, smoking and social alcohol use history presented with 2 days of recurrent nausea and vomiting and was admitted to the emergency department on September 26, 2024. Initial vital signs revealed severe hypertension (194/133 mmHg) and mild confusion (GCS E4V4M6). Emergency cranial CT demonstrated acute hemorrhage within the right lateral ventricle. (Figure 1) Emergent hematoma evacuation and external ventricular drainage (EVD) were performed on the same day, and perioperative antibiotic prophylaxis (cefuroxime 1.5g IV) was administrated afterwards. Postoperatively, he was transferred to the intensive care unit (ICU).

Clinical course and initial management

Perioperative antibiotic prophylaxis was cefuroxime (1.5g IV). On postoperative day 1 (POD1, Sep 27), due to fever (37.7°C) and rising inflammatory markers (White Blood Cell, WBC 15.44x10⁹/L), empirical therapy with ceftriaxone (2g IV qd) was initiated, alongside corticosteroids, gastroprotection, and nutritional support. Persistent fever and rising markers (Procalcitonin, PCT 0.32 ng/mL on Oct 3) prompted sequential antimicrobial escalations: piperacillin-tazobactam (4.5g IV q8h) on Oct 1, then addition of vancomycin (1g IV q12h via continuous infusion) on Oct 3. On Oct 6, he was transferred back to neurosurgery. CSF analysis (Oct 6) confirmed intracranial infection with yellow, turbid CSF; WBC 1800x10⁶/L (98% neutrophils); protein 1.6 g/L; glucose 2.4 mmol/L. Therapy was escalated to meropenem (2g IV q8h) plus vancomycin (1g IV q12h) and intrathecal vancomycin (20mg). Blood cultures drawn on October 7 reported growth of *Staphylococcus epidermidis* (β-lactamase positive) in one bottle on October 12, deemed a skin contaminant given ongoing piperacillin-tazobactam and vancomycin coverage. Serum *Mycoplasma pneumoniae* IgM was negative, IgG weakly positive on Oct 15, not suggestive of acute infection. Sputum cultures identified *Pseudomonas aeruginosa* on October 17 (susceptible to amikacin, intermediate to meropenem/polymyxin). The existing high-dose meropenem (2g IV q8h) was continued for pulmonary coverage, leveraging its optimized PK/PD profile against intermediately susceptible strains. Despite this, fever persisted (up to 40°C), and CSF parameters worsened (WBC rising to 2170x10⁶/L, glucose falling to 1.4 mmol/L on Oct 18). (Table 1)

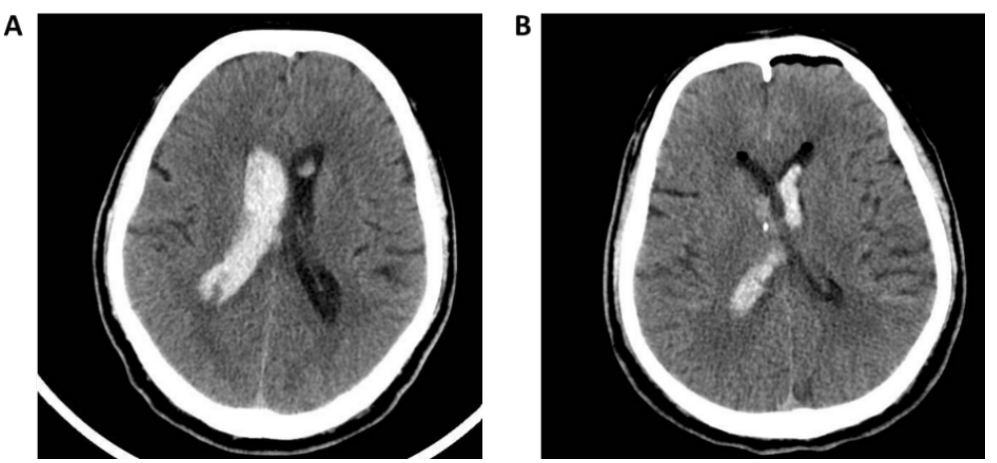

Figure 1. Head CT scans of the patient after admission in hospital. (A). Head CT showing a amount of blood, effusion, and swelling of the surrounding soft tissue in the right lateral ventricle on September 26. (B). Head CT after intracerebral hemorrhage surgery on September 27.

Table 1: Progressive infection and empirical antimicrobial therapy (Sep 27 - Oct 17)

Date	27-Sep	29-Sep	1-Oct	3-Oct	6-Oct	7-Oct	8-Oct	11-Oct	15-Oct	17-Oct
Temp°C	37.7	38.4	38.5	38.1	38.2	39	39	39	38.2	38.6
WBC×10⁹/L	15.44	13.62	12.58	16.85	17.3	15.11	22.74	-	19.33	14.71
Neut×10⁹/L	13.51	12.17	11.34	14.26	14.98	11.66	19.2	-	16.8	11.98
PCTng/mL	<0.05	-	0.05	0.32	0.26	0.12	<0.1	<0.1	<0.1	0.1
CSF WBC×10⁶/L	-	-	-	-	1800	1800	2770	1500	3090	446
Pressure mmH_2O	-	-	-	-	290	-	-	-	-	-
Protein g/L	-	-	-	-	-	1.6	1.64	2.06	2.8	2.71
Glucose mmol/L	-	-	-	-	-	2.4	2.7	2.5	2.1	1.7
Intervention	Ceftriaxone 2g IV qd initiated		Piperacillin-tazobactam 4.5g q8h	Vancomycin 1g IV q12h added	CSF: Yellow/ turbid;Meropenem 2g q8h + IV/IT Vancomycin 20mg		Ventriculostomy performed		CSF sent for mNGS	mNGS results received

Diagnostic breakthrough with mNGS

Due to persistent infection despite broad-spectrum therapy, CSF was sent for mNGS (MetaCAP™, KingMed Diagnostics, Guangzhou) on POD19 (Oct 15), with informed consent. Results returned on Oct 17, identifying *Mycoplasma hominis* with 232,424 sequence reads and 99% confidence. (Figure 2) Other microbial signals (e.g., Torque Teno Virus, 20 sequence reads) were classified under the "commensal microflora list" in the mNGS report, indicating low-abundance colonizing microorganisms without clinical significance. The failure of meropenem and vancomycin (both ineffective against mycoplasmas) corroborated the plausibility of *M. hominis* as the causative pathogen.

Therapeutic intervention and pharmacist role

Based on the mNGS result, the clinical pharmacist advised targeted anti-mycoplasma therapy. Considering intrinsic resistance profiles, blood-brain barrier penetration, and published case reports, therapy was changed on Oct 18 to moxifloxacin 0.4g IV qd and doxycycline 0.1g PO bid and IV/intrathecal vancomycin was stopped. Meropenem 2g IV q8h was discontinued on Oct 23, while amikacin 0.8g IV qd (targeting *P. aeruginosa* from sputum cultures) was maintained. Doxycycline was briefly paused (Oct 19–25) due to polypharmacy concerns but resumed given its critical role in the anti-mycoplasma regimen.

Clinical and laboratory response

Following the initiation of targeted anti-mycoplasma therapy with moxifloxacin and doxycycline on October 18, the patient exhibited rapid clinical improvement. Fever declined from a baseline of 38–40°C to 37.5°C by November 4. Cerebrospinal fluid (CSF) parameters resolved significantly: CSF white blood cell (WBC) counts decreased from 7,320 × 10^6/L on October 19 to 55 × 10^6/L by October 30–31, while CSF glucose levels recovered from 0.9 mmol/L to 4.4 mmol/L. CSF appearance transitioned from turbid to clear. Peripheral inflammation markers normalized, with blood WBC decreasing to 7.66 × 10^9/L. This resolution validated both the *Mycoplasma hominis* diagnosis and the efficacy of the targeted antimicrobial regimen. (Table 2)

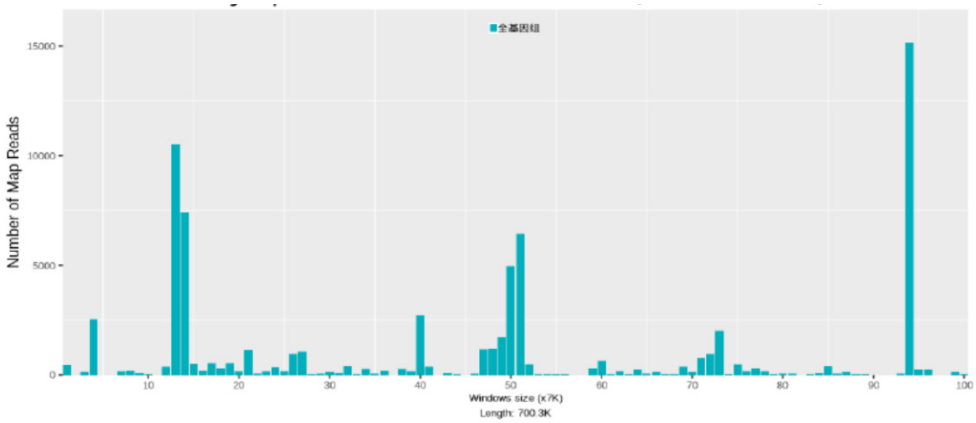

Figure 2. mNGS analysis reveals the mapping and distribution of M. hominis reads. Mapping of *M. hominis* reads on the genome with a coverage of 16.28%.

DISCUSSION

Postoperative CNS infections are predominantly caused by typical pathogens such as *Staphylococcus aureus*, coagulase-negative staphylococci, *Enterobacteriaceae*, and *Pseudomonas aeruginosa.*[5] *M. hominis* CNS infection is common in neonates but rare in adults after craniocerebral surgery.[6] It has reported that open injury, hematogenous spread, ascending neurotropic invasion were the main means of CNS infections by *M. hominis*.[7] And patients who had cerebrospinal fluid leakage, ventricular drainage, multiple operations, surgical incision infection, and long operation time were at high risk of intracranial infection.[3] In this case, the risk of the following CNS infection after surgery was markedly increased due to the long operation time and external ventricular drainage tube.

The diagnosis of *M. hominis* remains challenging. This fastidious, cell wall-deficient bacterium evades Gram staining and yields nonspecific serological results – creating a perfect diagnostic blind spot that explains the therapeutic failure observed in this case despite escalating broad-spectrum therapy.[8] Mycoplasma culture is the golden method for the validation of mycoplasma infection. However, due to the lack of special liquid medium containing both arginine and cholesterol, most culture were negative.[9]

The alternate diagnostic approaches include mNGS, 16 S rDNA, and 16 S rRNA with CSF. The pivotal breakthrough came through mNGS, which identified *M. hominis* with 232,424 sequence reads – a result whose reliability was rigorously confirmed through technical validity (reads vastly exceeding background noise/contaminants), biological plausibility (explained prior β-lactam/vancomycin failure), therapeutic corroboration (rapid resolution of fever and CSF abnormalities post-targeted therapy), and exclusion of alternative pathogens. mNGS represents a transformative, hypothesis-free diagnostic tool that enables comprehensive detection of pathogens (bacterial, viral, fungal, parasitic) and antimicrobial resistance genes directly from clinical specimens. By circumventing the need for cultivation, mNGS has proven particularly valuable in diagnosing challenging infections, such as culture-negative sepsis, unexplained encephalitis, and infections in immunocompromised hosts. mNGS offers direct genomic sequencing of specimens, markedly reducing turnaround time and improving detection rates.[10] While mNGS offers unparalleled advantages in detecting atypical/uncultivable pathogens within 48 hours, its clinical adoption faces practical barriers, primarily high cost and interpretive complexity regarding low-abundance signals.[11] Nevertheless, its value for culture-negative, treatment-refractory CNS infections is undeniable. *M. hominis* CNS infection diagnosed by mNGS technology has been reported in some cases, especially in neonate.[12] Since mycoplasma meningitis after neurosurgery is rare it has been reported in adults mNGS was recommended to detect *M. hominis* in the CSF and then provide targeted treatment.[13]

Empirical antimicrobial regimens invariably target typical pathogens, mainly combining β-lactams (e.g., ceftriaxone, ceftazidime

Table 2: Therapeutic response (Oct 18 - Nov 5)

Date	18-Oct	19-Oct	20-Oct	21-Oct	22-Oct	23-Oct	24-Oct	26-Oct	27-Oct	30-Oct	31-Oct	4-Nov	5-Nov
Temp°C	38	38.4	38.2	38.4	39.2	38.5	38.7	38.2	37.8	38.8	38.5	37.5	37.6
WBC×10^9/L	-	-	9.75	-	-	-	6.68	-	8.53	7.66	-	-	-
Neut×10^9/L	-	-	7.73	-	-	-	4.49	-	6.1	5.6	-	-	-
PCT ng/mL	-	-	<0.1	-	-	-	<0.1	-	<0.1	0.13	<0.1	-	-
CSF Appearance	Yellow/turbid	Orange/ turbid	Yellow/ turbid	Yellow/ turbid	Yellow/ turbid	Yellow/ clear	Yellow/ clear	Yellow/ clear	Yellow/ clear	Yellow/ clear	Colorless/ clear	-	-
CSF WBC ×10^6/L	22170	7320	6400	323	45	134	60	94	76	70	55	-	-
Pressure mmH2O	-	-	-	-	-	-	-	-	-	-		-	-
Protein g/L	3.06	3.51	3.34	3.26	3.08	2.87	3.03	2.26	2.51	2.09	1.97	-	-
Glucose mmol/L	11.4	0.9	1.2	5.2	5.5	5	6.2	3.6	4	4.4	4.4	-	-
Key Event	Targeted therapy STARTED:Moxifloxacin 0.4g IV qd +Doxycycline 0.1g PO bid;Vancomycin stopped	Doxy-cycline paused (poly-pharmacy concern)				Merope-nem stopped		Doxy-cycline resumed					Trans-ferred for rehabili-tation

or meropenem) with glycopeptides like vancomycin.[14] Non-classical pathogens like *Mycoplasma hominis*, however, rarely enter clinical consideration due to their extremely low incidence, absence from major guideline recommendations, and diagnostic invisibility.[15] Critical to therapeutic success was the intervention of the clinical pharmacist, who translated the mNGS result into precision antimicrobial selection. Tetracyclines (including doxycycline, tetracycline and minocycline) interfere with protein synthesis and are commonly used to treat mycoplasmas, so are the quinolones (including moxifloxacin, ciprofloxacin, and levofloxacin) which inhibit DNA replication.[16] Moxifloxacin was prioritized for its potent anti-mycoplasma activity combined with high CSF penetration (>50% serum levels), while doxycycline was added for synergy despite limited CNS pharmacokinetic data. Significantly, azithromycin was avoided despite sporadic reports of efficacy in neonatal CNS mycoplasma infections, primarily due to its extremely low CSF penetration (<5%) compromising its reliability for intracranial infection.

In the cases reviewed, 5 patients treated with tetracycline and quinolone after the pathogen was confirmed as *M. hominis* were cured[3]. The dramatic clinical and laboratory response to the chosen regimen (CSF WBC decreased from 7,320 to 55 $\times 10^6$/L, glucose normalized from 0.9 to 4.4 mmol/L) provided compelling evidence validating both the pathogen identification and the pharmacotherapeutic strategy. While isolated case reports suggest azithromycin may have immunomodulatory effects contributing to clinical benefit, its role in CNS mycoplasma infections remains poorly supported by pharmacokinetic principles and warrants further investigation in larger cohorts.[17] Therefore, the combination use of both tetracycline and quinolone seems to be a good choice for the treatment of *M. hominis*. This study has several limitations. First, the findings are based on observations from a single patient, which precludes any generalization to broader populations or the establishment of causal relationships. Second, although we conducted a comprehensive diagnostic workup, the possibility of unmeasured confounding factors or alternative explanations for the clinical course cannot be entirely ruled out. Finally, as this is a retrospective description, our insights are constrained by the available clinical data and documentation. Despite these limitations, we believe this case provides valuable mechanistic clues and serves as an important educational alert for similar clinical scenarios.

In conclusion, this case illuminates *M. hominis* as a formidable, albeit rare, cause of post-neurosurgical intracranial infection. Although it is effectively invisible to conventional diagnostic methods, it is detectable by mNGS, illustrating the clinical significance of mNGS in the diagnosis of nonclassical CNS infection. The synergy between mNGS and specialized clinical pharmacy expertise was pivotal, enabling a critical shift from failing empirical therapy to successful, pathogen-directed treatment with moxifloxacin and doxycycline, resulting in rapid clinical and laboratory resolution. While challenges related to cost and interpretation complexity persist, mNGS has proven indispensable for the diagnosis of culture-negative CNS infections where conventional approaches falter. We advocate for the early application of mNGS in cases of post-neurosurgical infection showing persistent signs of inflammation (e.g., fever, elevated CSF WBC) despite 72 hours of appropriate empirical antimicrobial therapy. Furthermore, mandatory involvement of clinical pharmacists is crucial to optimize antimicrobial selection based on confirmed pathogen profiles, CNS penetration data, and antimicrobial stewardship principles. Finally, agents like azithromycin should be used cautiously for CNS mycoplasma infections, reserved for situations where first-line options with proven CNS penetration (fluoroquinolones, tetracyclines) are contraindicated, acknowledging its suboptimal pharmacokinetic profile in this compartment.

DISCLOSURE

Ethics: This work has been approved by the ethical committees of the Affiliated Shunde Hospital of Jinan University (No.JDSY-LL-2025012). Consent for publication was obtained by participant in this study.

Data availability: The data that support the findings of this study are available on request from the corresponding author.

Financial support: This work was supported by Science and Technology Innovation Project of Foshan (No.2420001004141).

Conflicts of interest: None

REFERENCES

1. Li M, Meng W, An L, *et al*. Comparative effectiveness of monotherapy vs. combination therapy for postoperative central nervous system infections in neurosurgical patients: a retrospective cohort study. *BMC Infect Dis* 2025;25(1):644. doi: 10.1186/s12879-025-11031-0.
2. Moridi K, Hemmaty M, Azimian A, *et al*. Epidemiology of genital infections caused by Mycoplasma hominis, M. genitalium and Ureaplasma urealyticum in Iran; a systematic review and meta-analysis study (2000-2019). *BMC Public Health* 2020;20(1):1020. doi: 10.1186/s12889-020-08962-5.
3. Gao X, Guo Y, Luo P, Su J, Yao Z. Central nervous system infection caused by *Mycoplasma hominis* in an adult: a case report and literature review. *Eur J Clin Microbiol Infect Dis* 2025;44(11):2695-703.doi: 10.1007/s10096-025-05228-z.
4. Han D, Li Z, Li R, Tan P, Zhang R, Li J. mNGS in clinical microbiology laboratories: on the road to maturity. *Crit Rev Microbiol* 2019;45(5-6):668-85. doi: 10.1080/1040841X.2019.1681933.
5. Hu J, Yu W, Cui J, Zhang L, Yu W. Recent advances in diagnostic technologies for postoperative central nervous system infections: a review. *Neurol Sci* 2025;46(9):4279-91. doi: 10.1007/s10072-025-08279-4.
6. Waites KB, Rudd PT, Crouse DT, *et al.* Chronic *Ureaplasma urealyticum* and *Mycoplasma hominis* infections of central nervous system in preterm infants. *Lancet* 1988;1(8575-6):17-21. doi: 10.1016/s0140-6736(88)91002-1.
7. Yang NL, Cai X, Que Q, Zhao H, Zhang KL, Lv S. *Mycoplasma hominis* meningitis after operative neurosurgery: A case report and review of literature. *World J Clin Cases* 2022;10(3):1131-9. doi: 10.12998/wjcc.v10.i3.1131.
8. Liu Y, Tang J, Wang Y, Cui F, Yang Y. Intracranial infection caused by *Mycoplasma hominis* after neurosurgical operation: an easily overlooked but serious condition. *J Infect Dev Ctries* 2025;19(9):1425-31. doi: 10.3855/jidc.20729.
9. Lee EH, Winter HL, van Dijl JM, Metzemaekers JD, Arends JP. Diagnosis and antimicrobial therapy of Mycoplasma hominis meningitis in adults. *Int J Med Microbiol* 2012;302(7-8):289-92. doi: 10.1016/j.ijmm.2012.09.003.
10. Che G, Liu F, Chang L, Lai S, Teng J, Yang Q. *Mycoplasma hominis* meningitis diagnosed by metagenomic next-generation sequencing in a preterm newborn: A case report and literature review. *Lab Med* 2023;54(1):e24-e28. doi: 10.1093/labmed/lmac078.
11. Cai S, Pan J, Wang S, *et al.* Accurate etiological diagnosis of *Mycoplasma hominis* mediastinitis in immunocompetent patients using metagenomic next-generation sequencing: a case series and literature review. *J Thorac Dis* 2024;16(4):2499-509. doi: 10.21037/jtd-24-286.
12. Xi M, Cui S, Zhong YL, *et al*. Meningitis in neonate caused by *Mycoplasma hominis*: A case report. *Heliyon* 2023;10(1):e23489. doi: 10.1016/j.heliyon.2023.e23489.
13. Dong Y, He Y, Zhou X, *et al.* Diagnosis of *Mycoplasma hominis* meningitis with metagenomic next-generation sequencing: A case report. *Infect Drug Resist* 2022;15:4479-86. doi: 10.2147/IDR.S371771.
14. O'Horo JC, Sampathkumar P. Infections in neurocritical care. *Neurocrit Care* 2017;27(3):458-67. doi: 10.1007/s12028-017-0420-9.
15. Whitson WJ, Ball PA, Lollis SS, Balkman JD, Bauer DF. Postoperative *Mycoplasma hominis* infections after neurosurgical intervention. *J Neurosurg Pediatr* 2014;14(2):212-8. doi: 10.3171/2014.4.PEDS13547.
16. McCarthy KL, Looke DF. Successful treatment of post-neurosurgical intracranial *Mycoplasma hominis* infection using gatifloxacin. *J Infect* 2008;57(4):344-6. doi: 10.1016/j.jinf.2008.06.022.
17 . Che G, Liu F, Chang L, Lai S, Teng J, Yang Q. *Mycoplasma hominis* meningitis diagnosed by metagenomic next-generation sequencing in a preterm newborn: a case report and literature review. *Lab Med* 2023;54(1):e24-e28. doi: 10.1093/labmed/lmac078.