

Successful Treatment of Extensively Drug-Resistant *Acinetobacter baumannii* Intracranial Infection with Meropenem and Cefoperazone Sodium Sulbactam: A Case Report

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Background: *Acinetobacter baumannii* intracranial infections, especially those caused by multidrug-resistant (MDR) or extensively drug-resistant (XDR) strains, have posed an increasing challenge to treatment because of poor drug permeability through the blood–brain barrier (BBB) and increased bacterial drug resistance. Therefore, we aimed to explore a therapeutic schedule for *Acinetobacter baumannii* intracranial infection.

Case Presentation: We reported a case of intracranial infection caused by XDR *A. baumannii* after severe traumatic brain injury, cerebrospinal fluid (CSF) rhinorrhea, and severe pneumonia that was successfully treated with meropenem and cefoperazone sodium sulbactam.

Conclusion: This case illustrated that meropenem combined with cefoperazone sodium sulbactam could still be a therapeutic option against intracranial XDR *A. baumannii* infection.

Keywords: intracranial infection, *Acinetobacter baumannii*, extensively drug-resistant, meropenem, cefoperazone sodium sulbactam

Introduction

Acinetobacter baumannii intracranial infection is a serious infectious disease of the central nervous system, and its incidence is gradually increasing worldwide, with an associated mortality rate ranging from 15% to 71%, which suggests poor prognosis.^{1,2} Because of the increased drug resistance rate and poor drug permeability through the blood–brain barrier (BBB), the choice of antibiotics is very limited, and treatment of intracranial infections caused by *A. baumannii* is becoming challenging.^{3,4}

The standard treatment for *A. baumannii* intracranial infections typically involves a combination of antibiotics, such as colistin, tigecycline, or carbapenems, often administered intravenously or via intrathecal injection to overcome the BBB. However, the emergence of extensively drug-resistant (XDR) *A. baumannii* strains has further complicated treatment strategies, as these strains are resistant to most conventional antibiotics. In such cases, combination therapy with high-dose intravenous antibiotics,^{5–7} such as meropenem and sulbactam, has been explored as a potential alternative, though evidence supporting its efficacy remains limited.

Here, we report a patient with extensive drug resistant (XDR) *A. baumannii* intracranial infection after severe traumatic brain injury. However, he was successfully cured by intravenous (IV) injection of meropenem and cefoperazone sodium sulbactam.

Case Presentation

A 61-year-old male patient was admitted to our hospital on November 12, 2023, with severe traumatic brain injury sustained after being struck on the head by a piece of wood while repairing his house and disturbances in consciousness 1 hour previously. The patient was in a coma when light red fluid flowed out from his nose slowly, which was confirmed to be cerebrospinal fluid (CSF) rhinorrhea through high glucose measurements, and the Glasgow coma score (GCS) was E2V3M4. Emergency head computed tomography (CT) revealed multiple brain contusions, severe skull base fractures, and pneumocephalus (Figure 1A). Chest CT revealed bilateral lung exudation, indicative of pneumonia, which was likely associated with CSF rhinorrhea following the traumatic brain injury (Figure 1B). The patient presented with significant sputum production and labored breathing, further supporting the diagnosis of pneumonia and highlighting the severity of his respiratory compromise. Ceftizoxime sodium (2 g IV q12h) was administered to prevent infection, and 250 mL of a 20% mannitol solution was given intravenously to reduce intracranial pressure every 12 hours. On the second day, the patient underwent tracheotomy, and the cuff was maintained at appropriate pressure to prevent continuous aspiration of CSF rhinorrhea. Five days after admission, the patient's nasal cavity became dry, and he had intermittent fever (peak at 38.4°C). Laboratory tests showed leukocytosis ($15.4 \times 10^9/L$) and an elevated C-reactive protein level (CRP, 282.0 mg/L). Additionally, the patient's first sputum culture was negative and showed no signs of meningeal irritation. Considering the above results, we did not adjust the antibiotic and repeated sputum cultures. Seven days after admission, the patient's fever did not improve, breathing gradually became difficult, and blood gas analysis revealed type I respiratory failure. Re-examination of the chest CT scan (Figure 2B) revealed increased bilateral lung exudation with consolidation. He was diagnosed with severe pneumonia and placed on ventilator-assisted breathing to support respiratory function, and the antibiotic was adjusted to meropenem 1 g IV q8h. Lumbar puncture was performed to rule out intracranial infection. The CSF was light red in color. The CSF white blood cell count (WBC) was $30 \times 10^6/L$, the red blood cell (RBC) count was full field of view, glucose was 3.95 mmol/L, and protein was 0.88 g/L (Table 1). Re-examination of the brain CT (Figure 2A) showed that the brain contusions were better than before, and the gas within the cranial cavity had been absorbed. Two sputum cultures indicated *staphylococcus aureus*, which was susceptible to all antibiotic drugs, except penicillin and erythromycin. Therefore, vancomycin (1 g IV q12h) was administered to resist infection. Four days later, the patient's condition improved significantly, with gradually decreasing temperatures and reduced inflammatory markers. The ventilator no longer needed to be persistently used and preparation for offline ventilation was initiated. In addition, he opened his eyes after sound stimulation and localized pain correctly, and the GCS score increased from E2V3M4 to E3VTM5, indicating that his consciousness also improved. On November 26, the patient was successfully weaned from the mechanical ventilator, and chest CT showed that pulmonary exudation and consolidation had significantly improved (Figure 3B). He was transferred to the neurosurgery ward for further treatment. The sputum culture became XDR *A. baumannii*, which was identified as colonization, with the consideration of improved respiratory



Figure 1 Brain and chest CT images. (A) Multiple brain contusions, skull fracture and pneumocephalus can be seen on admission; (B) Significant exudation was seen in the lower lobe of both lungs on admission.

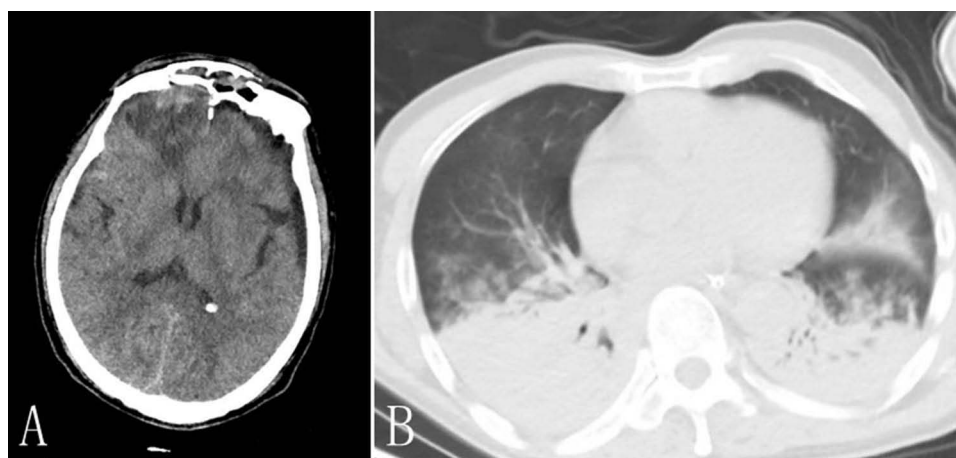


Figure 2 Brain and chest CT images. **(A)** On November 19, brain contusions were better than before, and the intracranial gas had been absorbed; **(B)** Increased bilateral lung exudation with consolidation on November 19.

symptoms and significantly decreased CRP (5.99 mg/L). Meropenem and vancomycin were subsequently discontinued, and the antibiotic was adjusted to ceftizoxime sodium (2 g IV q12h).

On November 29, the patient had a high fever (peak at 38.9°C) again with increased inflammatory markers and signs of meningitis. The CSF was obviously turbid, CSF WBC increased to $1,914 \times 10^6/\text{L}$, glucose was 0.53 mmol/L, and protein was 2.41 g/L. Brain CT reexamination indicated an absorbed hematoma and reduced cerebral edema, compared with before (Figure 3A). The patient was considered to have an intracranial infection; therefore, the antibiotic regimen was empirically adjusted to meropenem 2 g IV q8h and vancomycin 1 g IV q12h. Meropenem was pumped continuously using a micropump for 4 hours. On December 3, the patient's body temperature gradually dropped to 38.0°C, blood WBC returned to normal, and CRP dropped to 17.34 mg/L. CSF analysis showed WBC was $590 \times 10^6/\text{L}$, glucose was 1.71 mmol/L, and protein was 2.13 g/L. CSF culture indicated XDR *A. baumannii* which was susceptible only to colistin (Table 2). Because colistin was not available in our hospital and the patient was very poor, we changed the regimen to meropenem (2 g q8h) combined with cefoperazone sodium sulbactam (3 g q6h) under the advice of a clinical pharmacist. After 4 days, his body temperature returned to normal, and CSF analysis showed significant improvement; however, the CSF culture was still positive. On December 11, the CSF culture became negative with further decreased WBC and increased glucose, and his consciousness further improved; the GCS score increased from E3VTM5 to E4VTM6, then the tracheostomy tube was removed. Five days later, the CSF cultures were still negative, and the results of the CSF analysis returned to normal, therefore meropenem was discontinued and cefoperazone sodium sulbactam was reduced to 3 g q12. Intravenous antibiotics were discontinued 1 week later, and the patient recovered well and was discharged.

Follow-Up

At the 8-month follow-up, the patient demonstrated significant recovery, achieving normal levels of cognitive and physical function, as well as the ability to resume routine daily activities.

Table 1 Laboratory Tests of CSF in the Case

Date	November 20	November 29	December 3	December 7	December 11	December 16
WBC ($\times 10^6$)	30	1914	590	70	20	8
Glu (mmol/L)	3.95	0.53	1.71	3.17	3.38	3.34
Protein (g/L)	0.88	2.41	2.13	1.57	1.29	0.54

Abbreviations: CSF, cerebrospinal fluid; WBC, white blood cell.



Figure 3 Brain and chest CT images. **(A)** On November 29, brain CT indicated absorbed hematoma and reduced cerebral edema; **(B)** Pulmonary exudation and consolidation were significantly improved on November 26.

Discussion

Here, we report the case of a patient with XDR *A. baumannii* intracranial infection who was successfully treated with meropenem and cefoperazone sodium sulbactam. To the best of our knowledge, the clinical use of intravenous cefoperazone/sulbactam combined with meropenem for the treatment of XDR *A. baumannii* intracranial infection has not been previously reported. Owing to the increasing drug resistance of *A. baumannii*, anti-infective treatment options are becoming increasingly limited. In this situation, our success suggests that the therapeutic regimen of meropenem combined with cefoperazone sodium sulbactam should not be ignored despite XDR *A. baumannii* intracranial infection.

A. baumannii, which is related to intracranial infection after craniocerebral surgery or traumatic brain injury, has increasingly been considered as one of the main nosocomially acquired pathogens. Statistical data indicated that intracranial infection caused by *A. baumannii* accounted for 3.6–11.2% of all such infections,^{2,8} and the associated mortality rate could reach up to 71%.⁹ Increase in age, operation treatment, postoperative drainage time (≥ 3 days), postoperative hospital stay (≥ 10 days), a history of intensive care unit (ICU) stay, CSF leakage, the application of high-dose corticosteroids, and the use of antibacterial drugs are risk factors.^{8,10,11} The average infection time of *A. baumannii* is 12 days (range within 40 days).¹ In our case, the time for the development of XDR *A. baumannii* in CSF was 17 days, which is consistent with the time range reported in the literature. Over the past couple of decades, the drug resistance rate of *A. baumannii* has also increased obviously. According to the latest China Antimicrobial Surveillance Network (CHINET) data, the meropenem-resistant rate of *A. baumannii* has risen from 39.0% in 2005 to 72.7% in 2024.¹²

Table 2 Bacterial Culture and Antibiotics Susceptibility Tests for *A. baumannii* in CSF

Antibiotics	MIC ($\mu\text{g/mL}$)	Drug Sensitivity
Cotrimoxazole	≥ 16	R
Colistin	≤ 0.5	S
Cefoperazone/sulbactam	≥ 64	R
Cefepime	≥ 32	R
Imipenem	≥ 16	R
Meropenem	≥ 16	R
Ceftazidime	≥ 64	R
Tobramycin	≥ 16	R
Piperacillin/tazobactam	≥ 128	R
Doxycycline	≥ 16	R

Abbreviations: CSF, cerebrospinal fluid; MIC, minimum inhibitory concentration; R, resistant; S, susceptible.

National Healthcare Safety Network (NHSN) and Eurofins surveillance data revealed that more than 50% of *A. baumannii* was carbapenem-resistant in ICU isolates in the United States.^{4,13,14} More seriously, in some cases polymyxin was the only susceptible antibiotic against meningitis pathogens in some cases.¹⁵ Recently, Qin et al indicated the sensitivity of tigecycline against XDR *A. baumannii* was decreased.¹⁶ The use of broad-spectrum antibiotics, long-term ventricular drainage after neurosurgery, mechanical ventilation, and length of stay in the ICU are risk factors for the generation of drug-resistant bacteria.¹⁷ In the face of growing infection rates and drug resistance rates, treatment of *A. baumannii* intracranial infection, especially those caused by XDR or pandrug-resistant (PDR) strains, has become increasingly challenging.

In the present case, the patient suffered severe traumatic brain injury and CSF rhinorrhea. Considering no history of vomiting, short onset time, significant CSF rhinorrhea, and typical bilateral lung exudation, pneumonia associated with CSF rhinorrhea was confirmed, and ceftizoxime sodium was administered for anti-infection. Pneumonia associated with CSF rhinorrhea has rarely been reported. Most patients present with nonspecific respiratory symptoms, such as cough, expectoration, and dyspnea. Airway-centered ground glass opacities and a tendency of lower lobe predominance are typical imaging findings of chest CT,^{18,19} which is in line with our case.

As a result of traumatic brain injury, impaired consciousness is the most common symptom, which is one of the important risk factors of pneumonia.²⁰ Some studies have shown that early tracheotomy significantly shortened ICU stay and total hospitalization, and reduced the risk of pneumonia.^{21,22} In this case, considering the obvious CSF rhinorrhea and disturbances in consciousness, tracheotomy was performed on the second day after admission. Subsequently, CSF rhinorrhea stopped, but the patient developed fever and respiratory failure, with increased bilateral lung exudation and elevated inflammatory markers, suggesting that the pneumonia had deteriorated. The antibiotic was empirically adjusted to meropenem, and vancomycin was used in combination when sputum cultures indicated *staphylococcus aureus*. The patient's condition gradually improved and the pneumonia resolved.

However, the patient had a high fever again, combined with increased inflammatory markers, obvious signs of meningeal irritation, increased WBC count, and reduced CSF glucose levels. Therefore, intracranial infection was considered. Meropenem combined with vancomycin was empirically used for anti-infective treatment. XDR *A. baumannii* was cultured from the CSF, which was susceptible only to colistin. Unexpectedly, the patient's fever and inflammatory marker levels significantly improved, indicating that the current treatment was effective. We analyzed how the administration of a large dose and prolonged infusion may work. Considering that it was ineffective against gram-negative bacilli, vancomycin was replaced with cefoperazone sodium sulbactam.

Colistin was the only sensitive antibiotic in our case. The polymyxin family contains mainly polymyxin B and colistin (polymyxin E), which have been used since the 1950s. Owing to its high molecular weight, polymyxin cannot penetrate the BBB to reach the effective concentration required to kill bacteria. Many recent studies have indicated that intraventricular (IVT)/intrathecal (ITH) colistin and polymyxin B have a good clinical effect on intracranial infections caused by MDR or XDR *A. baumannii*.^{2,23–25} However, considering the severe neurotoxicity, such as chemical ventriculitis, chemical meningitis, seizures, and horsetail nerve syndrome, its application remains limited. In addition, polymyxin was not available at our hospital, and the patient could not afford the huge expenses of polymyxin. Many in vitro studies have shown that tigecycline exhibits strong antibacterial activity against *A. baumannii*. However, owing to its poor penetration through the BBB, intravenous tigecycline has no significant effect on intracranial infections caused by *A. baumannii*. Ni et al showed tigecycline in treating MDR-*A. baumannii* infection was associated with higher in-hospital mortality and lower microbial eradication rate, and compared with monotherapy, tigecycline combination therapy did not affect mortality, clinical response, or microbiological response.²⁶ In recent years, some studies have reported successful treatment XDR *A. baumannii* intracranial infection by IVT/ITH tigecycline.^{9,27–29} In our patient, because it was not available in our hospital during the treatment period, and due to its invasiveness and potential risks of infection and treatment controversy, IVT tigecycline was not considered. Surprisingly, when the treatment regimen was adjusted to meropenem combined with cefoperazone sodium sulbactam, the patient's body temperature gradually returned to normal and the number of WBC in the CSF obviously decreased, suggesting that the scheme was effective. Finally, the infection was successfully controlled.

Therefore, in the face of XDR *A. baumannii* intracranial infections, the therapeutic schedule of meropenem combined with cefoperazone sodium sulbactam should be reconsidered. Meanwhile, during the course of treatment, multiple monitoring parameters, such as routine blood tests, CRP, and CSF analysis, need to be intermittently performed to confirm the treatment effect of the schedule.

Conclusions

In conclusion, meropenem combined with cefoperazone sodium sulbactam could still be a therapeutic option against intracranial XDR *A. baumannii* infections. However, a case report primarily lies in its reliance on a single case, which lacks generalizability and representativeness, more research is needed to confirm the effectiveness of this scheme.

Data Sharing Statement

The original data used in this study are available from the corresponding authors upon reasonable request.

Ethics Statement

This study was approved by the ethics committee of Baoji Central Hospital. Institutional approval for publication of anonymized clinical details was obtained from Baoji Central Hospital in accordance with local regulations and ethical guidelines, and the patient provided informed consent for the publication of this case.

Author Contributions

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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