

Intrathecal Colistin Treatment for Multidrug-Resistant *Acinetobacter baumannii* in Neurosurgical Meningitis: A Case Report

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Abstract

Background. Infections of the central nervous system may develop in patients with traumatic brain injury after the implant of external ventricular drainage catheters or after neurological surgeries.

Case. We report the case of a woman in her 50s who was admitted with a subarachnoid hemorrhage secondary to a ruptured aneurysm, for which she underwent a tube ventriculostomy with an external ventricular drain attached and developed neurosurgical meningitis. The cerebrospinal fluid culture showed the presence of multidrug-resistant *Acinetobacter baumannii*. Intrathecal delivery of 65,000 units of colistin methyl sodium twice daily with a clamp drain for 15 to 60 min after administration was used as treatment. After 72 hours of treatment, the patient's infection improved, and repeat cerebrospinal fluid culture showed no microbial growth

Conclusion. Intrathecal colistin can be used as a treatment for multidrug-resistant *A. baumannii* meningitis.

Keywords: Multi-drug-resistant *Acinetobacter baumannii*, Intrathecal, Colistin, Post-neurosurgical meningitis, case report

Introduction

Infections of the central nervous system (CNS) may arise in patients with traumatic brain injury following the placement of external ventricular drainage (EVD) catheters or, more generally, after any neurosurgical procedure. An infection rate ranging from 2% to 33% is associated with external ventricular drainage, one of the

and various independent risk factors have been identified. (1) Organisms causing shunt-associated infections generally stick to the device surface and develop biofilms, making clinical and laboratory diagnosis and treatment difficult. (3) Due to the rise of multidrug-resistant bacteria, such as *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*, treating CNS infections has become more challenging. Modifications to treatment, such as a more significant daily dose and prolonged or continuous administration, could increase antibiotic concentrations at the site of infection and promote pathogen clearance. In the event of therapeutic failure or infection caused by difficult-to-treat bacteria, direct antibiotic instillation into the cerebrospinal fluid (CSF) and intravenous antibiotic administration may aid in the resolution of infection. (2)

most common neurosurgical procedures. The incidence of shunt-associated infections ranges from 1% to 18%,

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We report the case of a 55-year-old woman who was admitted with a subarachnoid hemorrhage secondary to a ruptured aneurysm, for which she underwent tube ventriculostomy with an external ventricular drain (EVD) attached and developed neurosurgical meningitis. This report aims to determine the effectiveness of intrathecal colistin therapy for multidrug-resistant *A. baumannii* central nervous system (CNS) infections.

Case Presentation

A woman in her 50s presented with a history of abrupt-onset headache and loss of consciousness approximately three days prior to admission. She was a known hypertensive patient with poor adherence to maintenance medication. She had no history of diabetes, substance abuse (including smoking and alcohol consumption), or food and drug allergies.

The patient presented to the emergency room in a state of confusion and reporting a headache; she was responsive to verbal stimuli, was afebrile, normotensive, not exhibiting respiratory distress, and nuchal rigidity was observed during physical examination. The patient was diagnosed with subarachnoid hemorrhage resulting from a ruptured aneurysm. An emergency right frontal tube ventriculostomy was conducted, during which an external ventricular drain (EVD) was inserted at a pressure of 7 to 8 cmH₂O. A cerebral catheter angiogram (CCA) revealed a saccular aneurysm with several teats in the left posterior communicating artery oriented posteriorly (Figure 1). The aneurysm was roughly 4.7 mm x 5.6 mm, with a neck of 4.9 mm (Figure 2). Based on the CCA results, pterional craniotomy was performed by clipping the left posterior communicating artery. An EVD pressure of 0-1 cmH₂O was maintained.

The patient had signs of a systemic inflammatory response post-surgery such as a fever of 38.7°C, tachycardia at 110 bpm, and leukocytosis reaching 45,000 cells/uL. We eliminated other possible sources of infection including assessments of respiratory, urinary tract, abdominal, and soft tissue infections, through examination of the surgery site and chest X-ray, as well as blood and urine cultures. All other physical examinations were normal, including respiratory, cardiovascular, and gastrointestinal assessments, except for the presence of nuchal rigidity. The patient was transferred to the Neurosurgery Critical Care Unit due to the lack of improvement in clinical status. On hospital day 16, the patient developed recurrence of fever and had clonic

seizures, a ventricular tap gram stain and culture study was performed. Previous empiric treatment with oxacillin was replaced with vancomycin (1 g every 12 h) and ceftriaxone (2 g intravenous every 12 h). The patient's condition deteriorated on the following day. She developed tachypnea, tachycardia, and decreased sensorium; therefore, the patient required mechanical ventilation. The CSF culture then revealed multidrug-resistant *A. baumannii* that was sensitive only to colistin.

Treatment

The antibiotics were shifted to polymyxin with 1.5 million units of IV infusion over two hours as a loading dose, followed by 1 million units of IV infusion over one hour q12H. However, the patient showed persistence of febrile episodes and onset of hypotension. Thus, colistin methyl sodium (65,000 units) was administered intraventricularly twice daily with a clamp drain for 15-60 min.

Outcome and follow-up

After 7 days of intrathecal colistin treatment, the patient's infection improved, as evidenced by the absence of fever and decreased leukocyte count. The patient had spontaneous eye opening but with no regard. There was no recurrence of the seizure. A repeat CSF culture showed no microbial growth after 72 hours of incubation.

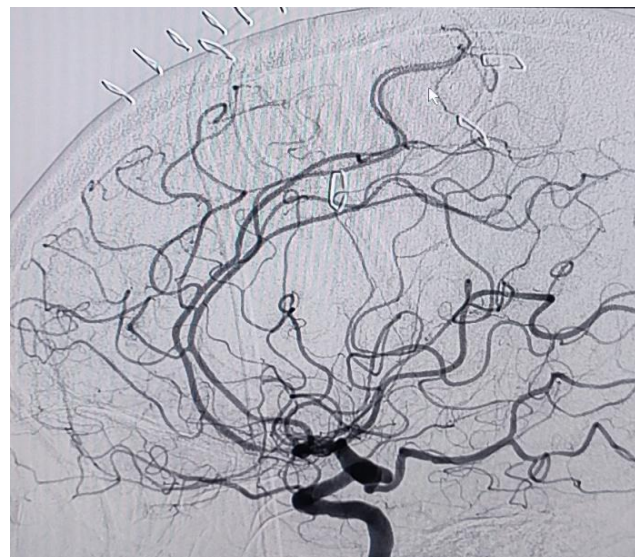


Figure 1. Cerebral catheter angiogram image of the patient with Left Internal Carotid Artery injections showing an aneurysm at the Left Posterior Communicating Artery



Figure 2. 3-dimension (3D) Rotational Angiography image of the patient showing a tortuous bovine type aortic arch and a saccular aneurysm at the Left Posterior Communicating Artery directed posteriorly

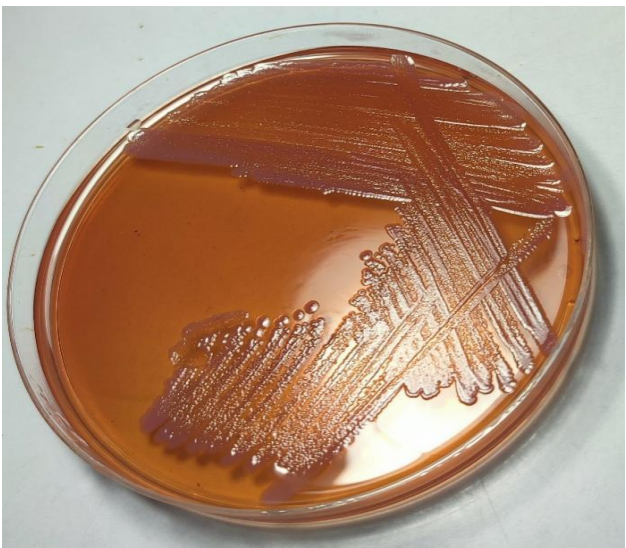
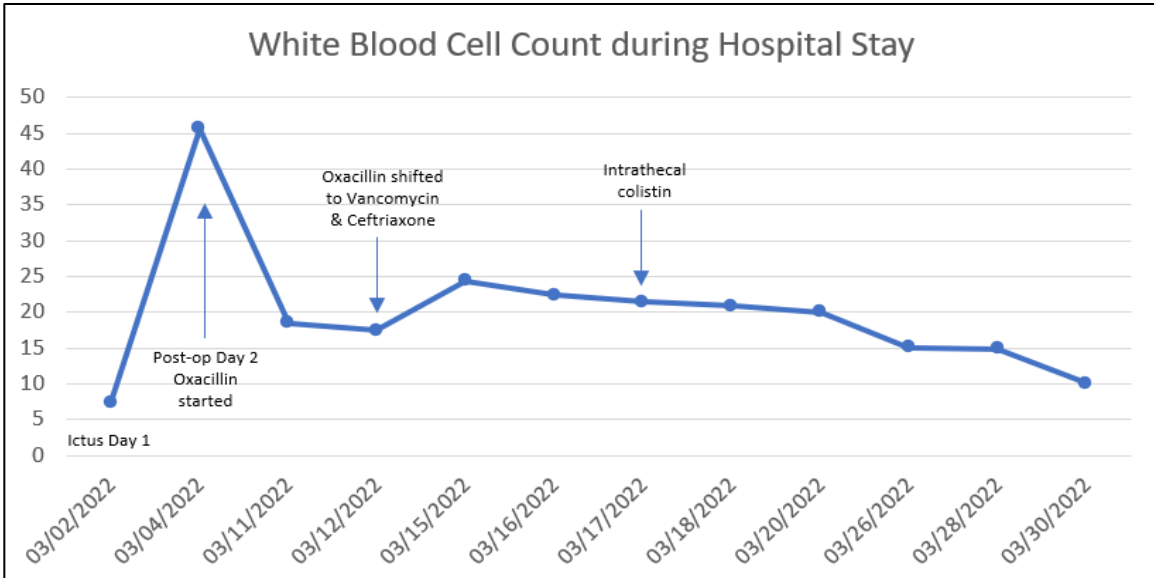


Figure 3. Opaque, raised, and creamy colonies of *A. baumannii* isolate of the patient on MacConkey Agar



Graph 1. White Blood Cell Count During Hospital Stay

Cerebrospinal Fluid Culture Study: Positive for <i>Acinetobacter baumannii</i> after 24 hours of incubation		
RESISTANT	INTERMEDIATE	SENSITIVE
Piperacillin-Tazobactam	Gentamicin	Colistin
Ceftazidime	Doxycycline	
Cefepime	Minocycline	
Imipenem		
Meropenem		
Amikacin		
Ciprofloxacin		
Cotrimoxazole		
Ampicillin-sulbactam		

Table 2: CSF Culture Study

Site of Positive Culture	<i>A. baumannii</i> strain	IT/IV colistin dose	IT/IV colistin duration	Concurrent Antibiotics	Time to CSF Sterilization
CSF	MDR	65,000 units	15-60 mins	Polymyxin	3 days

Table 3: Intrathecal Colistin Management

CSF – Cerebrospinal Fluid, MDR – multi-drug-resistant IT – intrathecal IV-intraventricular

Discussion

Meningitis after neurological surgery is a formidable challenge that results in severe morbidity, prolonged length of hospital stays, and increased hospital costs. (3) Significantly varied rates of meningitis caused by neurosurgery have been reported, ranging from 0.72 to > 8%. Despite the increasing advancements in neurosurgical technology and postoperative care, the meningitis rate following neurosurgery has remained relatively high in recent years.

CNS infections of external ventricular origin are significant complications of neurosurgical procedures. (6) Antimicrobial therapy for CNS infections should be based not only on the susceptibility of the isolated microbes but also on the drug's pharmacokinetic features, especially the passage of the molecule through the blood-brain barrier. Intrathecal colistin is an effective and safe treatment option for gram-negative bacteria resistant to multiple antibiotics.

A. baumannii has emerged as a significant multidrug- and pandrug resistant healthcare-associated pathogen. Several studies have reported outbreaks caused by multidrug-resistant *A. baumannii* with therapeutic effectiveness of aminoglycosides, carbapenems, β -lactamase inhibitors, tigecycline, rifampin, and colistin. Patients with CNS infections caused by colistin-susceptible *A. baumannii* isolates with pan-drug resistance may benefit from intrathecal or intraventricular colistin administration. Such regimen is based on the following notion: 1) intravenous colistin may not reach sufficient CNS penetration, 2) intravenous treatment failures have been observed, and 3) systemic treatment is associated with nephrotoxicity and neurotoxicity. (11) For multidrug-resistant *A. baumannii* meningitis, intrathecal colistin and aminoglycosides have been reported to have success rates above 80%. (12) A study revealed that the clinical and microbiological cure rates were above 80%. The commonly administered dose was 40,000-500,000 IU/day (1 mg of colistin equals 30,000 IU of colistin and 1 mg of colistimethate equals 12,500 IU of colistin), mixed with 0.9% sodium chloride, given once or twice daily through a ventricular catheter or a spinal needle after an equivalent volume of CSF was extracted. (13) Patients with EVD had their outflow stopped for 2 hours. The duration of therapy ranged from 2 to 3 weeks but could be changed according to clinical response, with CSF sterilization anticipated within 72 hours. (9) Owing to its poor pharmacokinetics, intravenous colistin

administration is recommended only for urinary tract infections or as inhalation therapy for multidrug-resistant bacterial infections. (14) However, colistin has been used off-label to sterilize the CSF in several studies. The dosages of antimicrobials have been empirical, with dose adjustments and dosing intervals mainly based on pharmacokinetic calculations to achieve adequate CNS concentrations. (15)

In a literature review, 7 and 17 cases of multidrug-resistant and pandrug-resistant *A. baumannii*, respectively, in a Thai Hospital revealed that the participants' mean age was 38 years (range 4-74 years), at least 12 of the 24 patients were women, and all (100%) were initially admitted for neurosurgical conditions. Most patients experienced either head trauma or intracranial bleeding. Among the 23 patients who underwent neurosurgery, 19 (83%) underwent craniotomy with EVD placement, 4 (17%) underwent tumor resection, 2 (9%) underwent dural grafting, and 1 (4%) underwent meningeal prosthesis placement. The median time from diagnosis to initiation of intrathecal or intraventricular colistin treatment was 2 days (range: 0-15 days), at a median dose of 150,000 IU/day (range: 40,000-500,000 IU/day) for the median duration of 15 days (range: 2-56 days). The clinical presentation of patients in the study included postoperative fever, altered mental status, headache, hypotension, and seizures. (16)

In this report, a woman with meningitis showed clinical improvement 72 hours after intrathecal colistin-CSF sterilization. Early recognition of bacterial infections and the start of effective antibiotic treatment, such as intrathecal colistin, can improve patient outcomes by decreasing the length and severity of the illness. However, the option to administer intrathecal colistin should be considered on a case-by-case basis, considering the specific type of infection and the patient's overall health status. In addition, it is essential to monitor for any potential side effects associated with intrathecal colistin administration and regulate treatment accordingly.

This case report highlights the use of intrathecal colistin for neurosurgical meningitis, demonstrating an unconventional but adaptable therapeutic strategy for managing MDR pathogens. This underscores the clinical innovation necessary for managing complex infectious diseases when standard therapies are ineffective. This approach is supported by empirical evidence and is consistent with existing literature on the use of intrathecal

antibiotics for central nervous system infections. This empirical basis enhances the credibility and scientific rigor of the selected treatment strategy. Stringent monitoring protocols are implemented to assess clinical response and adverse effects, highlighting a commitment to patient safety and careful management of potential complications related to intrathecal colistin therapy.

The report acknowledges limitations, particularly the specialized nature of intrathecal therapy, which necessitates substantial resources, including expertise in administration and monitoring, potentially lacking in various healthcare settings. This may restrict the broad implementation of this treatment approach. The variability in individual patient responses to intrathecal colistin complicates the prediction of treatment outcomes. This underscores the importance of individualized treatment strategies and meticulous patient selection to enhance therapeutic effectiveness.

Conclusion

Central nervous system infections may occur in patients having external ventricular drainage catheters. This case report highlights that intrathecal administration of colistin is an effective treatment for multidrug-resistant *A. baumannii* CNS infections, resulting in prompt sterilization of cerebrospinal fluid. Intrathecal colistin should be considered by physicians for CNS shunt infections caused by *A. baumannii*. In order to effectively treat CNS infections, antimicrobial therapy should prioritize both the pharmacokinetic properties and the susceptibility of the pathogens.

Conflict of Interest

The authors declare no conflict of interest relevant to this article.

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