World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(CASE REPORT)

Early healthcare-associated meningitis caused by new Delhi Metallo-β-Lactamase-Producing Enterobacter cloacae Complex Following Severe Traumatic Brain Injury: A case report and narrative review of the literature

Fouad Afkir *, Ayoub En-nasery, Reda Filali Baba, Ibrahim Bechri, Ali Derkaoui, Abdelkarim Shimi and Mohammed Khatouf

Department of Multidisciplinary Intensive Care, Hassan II University Hospital, Fez, Morocco.

World Journal of Advanced Research and Reviews, 2026, 31(02), 001–007

Publication history: Received on 20 June 2026; revised on 29 July 2026; accepted on 01 August 2026

Article DOI: https://doi.org/10.30574/wjarr.2026.31.2.2033

Abstract

Background: Healthcare-associated meningitis following severe traumatic brain injury (TBI) is an uncommon but life-threatening complication, particularly when caused by multidrug-resistant Gram-negative bacilli. New Delhi metallo-β-lactamase (NDM)-producing *Enterobacter cloacae* complex poses a major therapeutic challenge because of its extensive resistance to β-lactam antibiotics and the limited penetration of many antimicrobial agents into the central nervous system (CNS).

Case presentation: A 39-year-old previously healthy man was admitted following a road traffic accident resulting in severe TBI with bilateral extradural hematomas, frontotemporal cerebral contusions, multiple anterior skull base and facial fractures, and a probable osteodural breach associated with cerebrospinal fluid (CSF) rhinorrhea. On hospital day 4, persistent fever prompted lumbar puncture. CSF analysis revealed purulent meningitis characterized by marked neutrophilic pleocytosis, profound hypoglycorrhachia, and hyperproteinorrachia. CSF culture and multiplex polymerase chain reaction identified an NDM-producing *Enterobacter cloacae* complex. Targeted antimicrobial therapy consisted of high-dose extended-infusion meropenem, intravenous colistin following a loading dose, and adjunctive intrathecal colistin. Concomitant ventilator-associated pneumonia caused by *Klebsiella pneumoniae*, *Escherichia coli*, and multidrug-resistant *Acinetobacter baumannii* was treated with the same antimicrobial regimen. The patient became afebrile within 48 hours, repeat CSF cultures obtained on day 14 were sterile, and he was successfully extubated on day 14 with progressive neurological recovery to a Glasgow Coma Scale score of 12–13/15.

Conclusion: Early healthcare-associated post-traumatic meningitis caused by NDM-producing *Enterobacter cloacae* complex is rare but represents a major therapeutic challenge. Prompt microbiological diagnosis, rapid identification of resistance mechanisms, and individualized multidisciplinary management with optimized combination antimicrobial therapy, including intrathecal administration when appropriate, may improve clinical outcomes in these severe CNS infections.

Keywords: Healthcare-Associated Meningitis; Traumatic Brain Injury; *Enterobacter Cloacae* Complex; New Delhi Metallo-B-Lactamase (NDM); Carbapenemase-Producing Enterobacterales; Colistin; Intrathecal Therapy.

1. Introduction

Healthcare-associated meningitis and ventriculitis are serious infections of the central nervous system (CNS) that occur following neurosurgical procedures, traumatic brain injury (TBI) (1), placement of cerebrospinal fluid (CSF) shunts or external ventricular drains, or any condition associated with disruption of the meningeal barrier. In patients with severe

* Corresponding author: Fouad Afkir

TBI, skull base fractures, osteodural defects, and CSF leakage are well-established risk factors for post-traumatic meningitis (1,8) because they facilitate direct communication between the extracranial environment and the subarachnoid space.

The diagnosis of post-traumatic meningitis remains particularly challenging in the neurocritical care setting .(1,8) Clinical manifestations such as fever, impaired consciousness, CSF abnormalities, and elevated inflammatory markers may be attributed to the primary brain injury, intracranial hemorrhage, mechanical ventilation, or other healthcare-associated infections. Consequently, the diagnosis is often delayed, despite the fact that early microbiological confirmation and prompt initiation of appropriate antimicrobial therapy are critical determinants of clinical outcome .(1)

Enterobacter cloacae complex is an opportunistic Gram-negative pathogen that rarely causes meningitis outside the settings of neurosurgery (2,5,7), penetrating head trauma, intracranial devices, or disruption of the meningeal barrier. Treatment is further complicated by the organism's inducible chromosomal AmpC β-lactamase and its capacity to acquire additional resistance mechanisms, including extended-spectrum β-lactamases (ESBLs) and carbapenemases (6,10). Among these, New Delhi metallo-β-lactamase (NDM) is particularly concerning because it hydrolyzes nearly all β-lactam antibiotics, (10) including carbapenems, thereby severely limiting therapeutic options.

We report a rare case of early healthcare-associated meningitis caused by an NDM-producing *Enterobacter cloacae* complex that developed on the fourth day following severe traumatic brain injury in a patient with a probable osteodural defect and cerebrospinal fluid rhinorrhea. We also review the current literature regarding the diagnosis, antimicrobial management, and potential role of intrathecal colistin in the treatment of multidrug-resistant CNS infections.

2. Case Presentation

A 39-year-old previously healthy man was admitted to the emergency department following a road traffic accident resulting in severe traumatic brain injury (TBI) and associated left lower limb trauma.

On admission, his Glasgow Coma Scale (GCS) score was 13/15. Vital signs were as follows: heart rate 110 beats/min, blood pressure 100/50 mmHg, respiratory rate 20 breaths/min, and oxygen saturation 96% on room air. Neurological examination revealed bilaterally equal and reactive pupils, with no obvious focal motor or sensory deficit. Craniofacial examination showed bilateral periorbital ecchymosis, a left frontal wound, and otorrhea with rhinorrhea suggestive of cerebrospinal fluid (CSF) leakage. Beta-2 transferrin testing was not performed. Examination of the limbs revealed deformity of the left lower extremity. The remainder of the respiratory, cardiovascular, and abdominal examinations was unremarkable.

A whole-body computed tomography (CT) scan performed four hours after trauma revealed a left frontotemporal extradural hematoma associated with an ipsilateral temporal fracture line, left frontotemporal hemorrhagic contusions, and a right frontoparietotemporal extradural hematoma associated with an ipsilateral parietal fracture line. Multiple fractures involving the anterior skull base and facial bones were also identified, with findings suggestive of an osteodural defect. Follow-up brain CT scans performed at 12 hours and on day 2 showed stable intracranial lesions without indication for emergency neurosurgical intervention.

The initial clinical course was complicated by neurological deterioration, with a two-point decrease in the GCS score, requiring endotracheal intubation, mechanical ventilation, and initiation of neurocritical care measures. These included deep sedation, osmotherapy, prevention of secondary systemic insults, and non-invasive monitoring for intracranial hypertension using transcranial Doppler ultrasonography.

On hospital day 4, the patient developed persistent fever (39.5°C). A comprehensive infectious workup was performed. Peripheral and central blood cultures, as well as urine cultures, were negative. A protected distal respiratory sample isolated *Klebsiella pneumoniae*, β-lactam-susceptible *Escherichia coli*, and multidrug-resistant *Acinetobacter baumannii* susceptible only to colistin.

Given the history of severe head trauma with an osteodural defect and rhinorrhea suggestive of CSF leakage, lumbar puncture was performed. The CSF was cloudy on macroscopic examination. Cytological analysis demonstrated marked pleocytosis (18,900 cells/mm^3), predominantly neutrophilic (98%), associated with profound hypoglycorrhachia (0.05 g/L) and hyperproteinorrachia (8.5 g/L). Direct examination, conventional culture, and FilmArray®

meningitis/encephalitis multiplex PCR identified an NDM-producing *Enterobacter cloacae* complex carrying a carbapenemase resistance gene.

Following microbiological identification, antimicrobial therapy was adjusted to a combination regimen consisting of meropenem 2 g every 8 hours administered by prolonged infusion, intravenous colistin after a loading dose of 9 million international units (MIU), followed by 4.5 MIU every 12 hours, and intrathecal colistin at a dose of 125,000 IU/day. The total duration of targeted antimicrobial therapy was 15 days. The concomitant ventilator-associated pneumonia was managed with the same antimicrobial strategy.

The clinical course was favorable, with defervescence achieved within 48 hours. CSF rhinorrhea improved spontaneously, and immediate surgical repair of the osteodural defect was not required. A follow-up lumbar puncture performed on day 14 showed clear CSF with marked improvement of biological parameters: low residual cellularity, glucose concentration of 0.47 g/L, protein concentration of 0.79 g/L, chloride concentration of 118 mmol/L, and negative culture results.

The patient was successfully extubated on day 14, with favorable neurological evolution and a GCS score of 12–13/15. After completing 15 days of antimicrobial therapy, he was transferred to the neurosurgical department and subsequently scheduled for elective surgical management of the left lower limb fracture.

Table 1 Chronological summary of the case

Timing	Event	Main data
Day 0 - H4	Admission and injury assessment	TCG after AVP; GCS 13/15; CT/body CT: bilateral extradural hematomas, frontotemporal contusions, fractures of the anterior level of the facial mass, probable osteomeningeal breccia.
H12 then D2	CT Scan	Stability of intracranial lesions; absence of urgent neurosurgical indications.
Initial phase	Neuro-resuscitation	Neurological degradation of two points; intubation, mechanical ventilation, sedation, osmotherapy, prevention of ACSOS, transcranial Doppler monitoring.
Day 4	Persistent fever	Temperature 39.5 °C; negative blood cultures; ECBU negative; PPD positive for K. pneumoniae, E. coli and A. baumannii MDR.
Day 4	Initial lumbar puncture	Cloudy CSF; 18,900 elements/mm^3, 98% PNN; glucose 0.05 g/L; protein 8.5 g/L; Positive culture and FilmArray: Enterobacter cloacae complex with NDM gene.
D4-J15	Targeted therapy	Meropenem 2 g/8 h as an extended infusion; colistin IV loading dose 9 MIU then 4.5 MIU/12 h; intrathecal colistin 125,000 IU/day; total duration 15 days.
D6 approx.	Clinical Response	Apyrexia obtained in 48 hours; gradual improvement.
Day 14	LCR Control and Evolution	Clear CSF, negative culture, glucose 0.47 g/L, protein 0.79 g/L, chlorides 118 mmol/L; extubation on day 14; GCS 12-13/15.
Day 15	Orientation	Transfer to neurosurgery; Cold scheduled leg surgery.

Table 2 Evolution of cerebrospinal fluid parameters

Parameter	Initial LP (D4)	Control LP (J14)
Appearance	Trouble	Clear
Celularity	18,900 elements/mm^3, 98% PNN	Low residual cellularity; approx. 18 elements/mm^3 according to the report
Glycorachia	0.05 g/L	0.47 g/L
Proteinorachia	8.5 g/L	0.79 g/L

Chloride	Not specified	118 mmol/L
Direct examination/culture/PCR	Enterobacter cloacae complex; NDM gene detected by Multiplex FilmArray/PCR	Negative culture

2.1. Illustrations

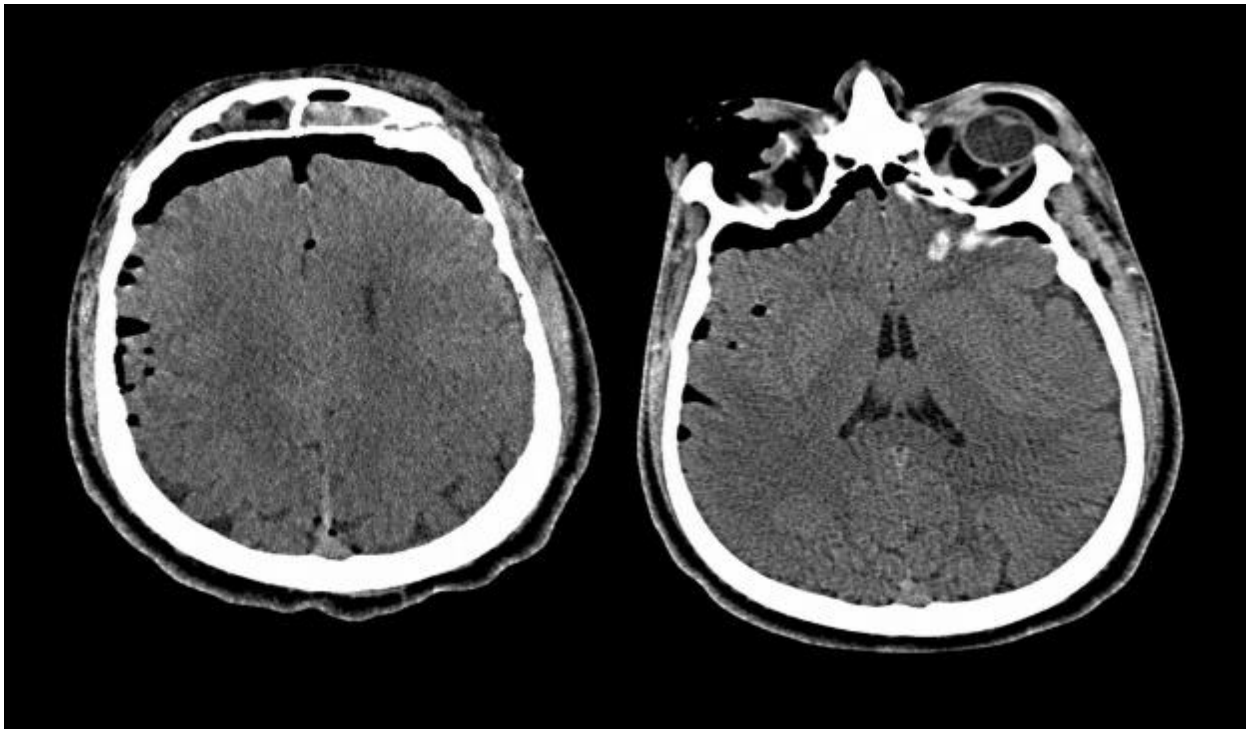

Figure 1 Initial brain CT, axial sections. Presence of frontal pneumoencephaly, associated with traumatic frontotemporal lesions in a context of fractures of the anterior level of the facial mass, suggestive of an osteomeningeal breach. These abnormalities explain the high risk of post-traumatic meningeal contamination.

3. Discussion

3.1. Particularities of post-traumatic meningitis

Post-traumatic meningitis represents a distinct entity among healthcare-associated central nervous system (CNS) infections (1,8). It usually results from disruption of the anatomical barrier between the upper respiratory tract and the meninges, particularly in the setting of skull base fractures, paranasal sinus fractures, osteodural defects, or cerebrospinal fluid (CSF) leakage. In our case, the initial rhinorrhea and otorrhea, associated with fractures involving the anterior skull base and facial bones, strongly suggested a meningeal entry point, despite the absence of confirmatory beta-2 transferrin testing.

The early onset of infection, occurring on hospital day 4, suggests that bacterial inoculation was facilitated by the anatomical defect, potentially compounded by exposure to the intensive care environment and mechanical ventilation. This early presentation differs from many cases of post-neurosurgical meningitis (1,2), which are frequently associated with implanted intracranial devices or recent surgical procedures.

3.2. Rarity and severity of *Enterobacter cloacae* complex meningitis

Meningitis caused by *Enterobacter cloacae* complex is uncommon in immunocompetent adults. Reported cases have mainly occurred in specific clinical settings, including neurosurgery, external ventricular drainage, traumatic brain injury, pneumocephalus, complicated otitis, or other conditions associated with disruption of the meningeal barrier. This pattern suggests that CNS infection by *E. cloacae* complex generally requires either anatomical disruption or iatrogenic alteration of the protective mechanisms of the CNS. (2,5,7)

The severity of these infections is related to several factors, including the critical illness context, delayed recognition due to overlapping neurological manifestations, and the limited penetration of several antimicrobial agents into the CSF (1,9). In our patient, the diagnosis was prompted by persistent unexplained fever, highly inflammatory CSF findings, and concordant identification of the pathogen by conventional culture and multiplex PCR.

3.3. NDM resistance mechanism and therapeutic implications

Enterobacter cloacae complex exhibits intrinsic resistance to several β-lactam antibiotics through inducible chromosomal AmpC β-lactamase production (6,10). Acquisition of an NDM-type carbapenemase (10) further compromises the antimicrobial profile, as metallo-β-lactamases hydrolyze carbapenems and are not inhibited by avibactam.

Current therapeutic options for invasive infections caused by NDM-producing Enterobacterales include combinations such as ceftazidime-avibactam plus aztreonam or cefiderocol (10), when available and active according to susceptibility testing. However, treatment choices remain highly dependent on local availability, antimicrobial susceptibility profiles, infection site, and pharmacokinetic considerations.

In our case, antimicrobial therapy consisted of high-dose meropenem administered by prolonged infusion, combined with intravenous colistin and intrathecal colistin. The use of meropenem against an NDM-producing strain remains controversial and should not be considered effective monotherapy. Nevertheless, carbapenems may occasionally be included in combination regimens depending on minimum inhibitory concentrations (MICs), bacterial inoculum, pharmacodynamic targets, and the absence of better therapeutic alternatives. Intrathecal colistin was selected because of the severity of the CNS infection, the multidrug-resistant profile of the pathogen, and the need to achieve adequate CSF concentrations. (10)

3.4. Role of intrathecal and intraventricular antimicrobial therapy

Intrathecal or intraventricular administration of antibiotics may be considered in multidrug-resistant Gram-negative CNS infections when systemic antimicrobial penetration is inadequate or when clinical and microbiological responses remain unsatisfactory (1,9). Current recommendations emphasize that this approach should be individualized and guided by antimicrobial susceptibility testing, expected CSF concentrations, neurological tolerance, and microbiological response.

Evidence supporting local antimicrobial administration remains limited and is mainly derived from retrospective studies and case reports. In the series reported by Tängdén et al. (3), the addition of intraventricular aminoglycosides to systemic therapy was associated with fewer relapses in Gram-negative neurosurgical ventriculitis and meningitis. Other reports have described favorable outcomes with intraventricular or intrathecal colistin in infections caused by carbapenemase-producing Enterobacterales. (5,4)

Our case illustrates the potential role of intrathecal colistin as a rescue strategy in a severe NDM-producing *Enterobacter cloacae* complex meningitis, with microbiological clearance of CSF documented on day 14.

3.5. Management of the osteodural defect

Persistent CSF leakage represents an important risk factor for recurrent meningitis. In our patient, rhinorrhea was not confirmed by beta-2 transferrin testing and resolved spontaneously, allowing surgical repair of the defect to be deferred. (1,8)

The decision regarding surgical closure should be individualized and discussed with neurosurgical and otolaryngological teams, taking into account the persistence of CSF leakage, risk of recurrent infection, neurological status, and anatomical characteristics of the defect.

Nevertheless, management of the anatomical portal of entry remains a key component of treatment. Recurrence of CSF rhinorrhea, persistent pneumocephalus, (8)or repeated infectious episodes should prompt reassessment for definitive surgical repair.

3.6. Comparison with the literature

The following table compares our case with relevant publications addressing *Enterobacter cloacae* complex meningitis, carbapenemase-producing Enterobacterales CNS infections, and Gram-negative meningitis or ventriculitis following neurosurgical procedures or trauma.

Table 3 Comparison with the literature

Author, year	**Background**	**Germ/profile**	**Reported treatment**	**Evolution**	**Interest in our case**
Briggs et al., 2004	Adult series after cranial surgery or trauma	Gram-negative bacilli meningitis	Appropriate treatment according to antibiogram	Significant morbidity	Closest context: surgery/trauma and BGN.
Tängdén et al., 2011	31 cases of neurosurgical ventriculitis/meningitis	Gram-negative bacilli	Systemic treatment ± intraventricular gentamicin	Fewer relapses with combined strategy	Argument to discuss the intraventricular/intrathecal route.
Cascio et al., 2014	Post-neurosurgical ventriculitis.	Enterobacter cloacae ESBL/carbapenemase	Intraventricular colistin	Favourable progress reported	Supports the use of local colistin in therapeutic impasses.
He et al., 2019	Severe meningitis	Enterobacter cloacae is highly resistant to carbapenems	Meropenem and IV Amikacin + Intraventricular Amikacin	Therapeutic success	Close case for multi-resistance and aggressive treatment.
Lee et al., 2023	Otogenic meningitis with pneumoencephaly	Enterobacter cloacae	Adapted antibiotic therapy	Evolution discussed in review	Shows the rarity of E. cloacae meningitis outside of a classical context.
Li et al., 2023	Review post-neurosurgical meningitis/ventriculitis	Carbapenem-resistant Enterobacteriaceae	Polymyxins, tigecycline, ceftazidime-avibactam/aztreonam, cefiderocol according to profiles	Heterogeneous data	Modern therapeutic framework for CNS CREs.
Our observation	Severe GCT with probable osteomeningeal breach; occurred on D4	Enterobacter cloacae complex NDM	Prolonged meropenem + IV colistin + intrathecal colistin 125,000 IU/d	Apyrexia 48 hours; Sterile CSF on day 14; extubation J14; GCS 12-13/15	Rare case combining post-traumatic precocity, NDM and favorable course under combined treatment.

Strictly post-traumatic meningitis caused by an NDM-producing *Enterobacter cloacae* complex remains exceptionally rare. Therefore, available comparisons include related cases involving *E. cloacae* complex meningitis, carbapenem-resistant Enterobacterales infections, and multidrug-resistant Gram-negative CNS infections occurring after neurosurgery or disruption of the meningeal barrier.

3.7. Strengths and limitations

The main strength of this case report is the exceptionally early occurrence of meningitis caused by an NDM-producing *Enterobacter cloacae* complex following severe traumatic brain injury with a probable osteodural defect. The microbiological diagnosis was strengthened by the concordant results of conventional culture and multiplex polymerase chain reaction, while the favorable clinical outcome achieved with combination antimicrobial therapy represents an additional noteworthy feature.

Several limitations should be acknowledged. First, CSF rhinorrhea was not confirmed by beta-2 transferrin testing, although the clinical and radiological findings strongly supported the presence of an osteodural defect. Second, detailed antimicrobial susceptibility data, including minimum inhibitory concentrations (MICs), were not available for retrospective analysis. Third, the individual contribution of each component of the combination antimicrobial regimen cannot be precisely determined. Finally, long-term neurological follow-up was not available at the time of manuscript preparation.

4. Conclusion

Early healthcare-associated meningitis caused by an NDM-producing *Enterobacter cloacae* complex following severe traumatic brain injury is a rare, severe, and therapeutically challenging complication. The presence of a probable osteodural defect, even without laboratory confirmation of CSF leakage, should prompt a high level of clinical suspicion for CNS infection in patients with unexplained fever in the neurocritical care setting.

Successful management requires a multidisciplinary approach combining early CSF sampling, rapid microbiological and molecular identification of the causative pathogen and resistance mechanisms, optimized antimicrobial therapy based on pharmacokinetic/pharmacodynamic principles, consideration of intrathecal or intraventricular administration in selected multidrug-resistant infections, and management of the anatomical source of infection.

This case suggests that early recognition, aggressive individualized treatment, and coordinated multidisciplinary care may result in favorable outcomes despite the presence of a highly resistant pathogen associated with limited therapeutic options.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] Tunkel AR, Hasbun R, Bhimraj A, et al. 2017 Infectious Diseases Society of America's Clinical Practice Guidelines for Healthcare-Associated Ventriculitis and Meningitis. Clinical Infectious Diseases. 2017; 64(6):E34-E65. doi:10.1093/cid/ciw861.

[2] Briggs S, Ellis-Pegler R, Raymond N, Thomas M, Wilkinson L. Gram-negative bacillary meningitis after cranial surgery or trauma in adults. Scandinavian Journal of Infectious Diseases. 2004; 36(3):165-173. doi:10.1080/00365540410019286.

[3] Tängdén T, Enblad P, Ullberg M, Sjölin J. Neurosurgical Gram-Negative Bacillary Ventriculitis and Meningitis: A Retrospective Study Evaluating the Efficacy of Intraventricular Gentamicin Therapy in 31 Consecutive Cases. Clinical Infectious Diseases. 2011; 52(11):1310-1316. doi:10.1093/cid/cir197.

[4] He Z, Wang C, Liu B, Feng M, Wang Z. Successful Treatment of Serious Meningitis Caused by Extremely Carbapenem-Resistant Enterobacter cloacae (MIC ≥16 mg/L) with i.v. Meropenem and i.v. Amikacin Plus Intraventricular Amikacin. Frontiers in Medicine. 2019;6:265. doi:10.3389/fmed.2019.00265.

[5] Cascio A, Conti A, Sinardi L, et al. Extended-spectrum beta-lactamase-producing and carbapenemase-producing Enterobacter cloacae ventriculitis successfully treated with intraventricular colistin. International Journal of Infectious Diseases. 2014;20:66-67. doi:10.1016/j.ijid.2013.11.012.

[6] Li C, Duan J, Wang H, et al. Treatment of Ventriculitis and Meningitis After Neurosurgery Caused by Carbapenem-Resistant Enterobacteriaceae (CRE): A Challenging Topic. Infection and Drug Resistance. 2023;16:3279-3294. doi:10.2147/IDR. S411312.

[7] Lee S, Kim S, Sunwoo JS. Otogenic Enterobacter cloacae meningitis complicated with pneumocephalus. Encephalitis. 2023; 3(4):125-128. doi:10.47936/encephalitis.2023.00164.

[8] La Russa R, Maiese A, Viola RV, et al. Post-Traumatic Meningitis Is a Diagnostic Challenging Time: A Systematic Review Focusing on Clinical and Pathological Features. International Journal of Molecular Sciences. 2020; 21(11):4148. doi:10.3390/ijms21114148.

[9] Nau R, Blei C, Eiffert H. Intrathecal Antibacterial and Antifungal Therapies. Clinical Microbiology Reviews. 2020; 33(3):E00190-19. doi:10.1128/CMR.00190-19.

[10] Tamma PD, Heil EL, Justo JA, Mathers AJ, Satlin MJ, Bonomo RA. Infectious Diseases Society of America 2024 Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections. Clinical Infectious Diseases. 2024; 79(3):e1-e110. doi:10.1093/cid/ciae403.