

***Citrobacter koseri* Meningitis in an Adult Patient: A Case Report and Literature Review**

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Abstract

Citrobacter koseri is a rare cause of bacterial meningitis, primarily affecting neonates and immunocompromised individuals. Meningitis in immunocompetent adults is exceptionally uncommon. We report a case of a 48-year-old male who developed *C. koseri* meningitis following nasal endoscopy for rhinosinusitis. He presented with headache, fever, vomiting, and altered mental status. CSF analysis suggested a bacterial infection, which was confirmed by the subsequent growth of *C. koseri* in culture. The patient was treated with IV and intrathecal antibiotics, leading to significant improvement and resolution of symptoms after 21 days. This case highlights the rare occurrence of *C. koseri* meningitis in an immunocompetent adult.

Keywords: *Citrobacter koseri*; Meningitis; Adult; Nasal endoscopy; Intrathecal therapy

Introduction

Citrobacter koseri, previously known as *Citrobacter diversus*, is an occasional cause of infections in neonates and immunocompromised patients. Neonates infrequently develop *C. koseri* meningitis and tend to develop central nervous system abscesses. Neonates who develop *C. koseri* meningitis are prone to developing central nervous system abscesses.¹ Meningitis caused by *C. koseri* in adults is extremely rare. Here, we report a case of *C. koseri* meningitis in an immunocompetent adult following an ENT procedure.

Case Report

A 48-year-old man was admitted to our hospital with persistent headache, fever, vomiting, and altered mental status. His symptoms started seven days prior to admission. He had recently undergone nasal endoscopy for rhinosinusitis. His medical history included essential hypertension, primary hypothyroidism, a resected pituitary adenoma two years prior, and recurrent deep venous thrombosis.

On admission, his body temperature was 38.0 °C, blood pressure was 131/78 mm Hg, heart rate was 82 beats per minute, respiratory rate was 18 breaths per minute, and oxygen saturation was 96% on ambient air. Neurological examination revealed somnolence, disorientation, nuchal rigidity, but no skin petechiae or cranial nerve abnormalities.

A computed tomography (CT) scan of the brain was normal. Blood levels of glucose, electrolytes, liver and kidney function, and coagulation tests were within normal ranges. Laboratory tests revealed an elevated C-reactive protein (CRP) level (337 mg/L) and a white blood cell count of 18 600/mm³.

A lumbar puncture (LP) performed within the first hour of admission showed purulent cerebrospinal fluid (CSF) with an elevated opening pressure (50 mmH₂O). CSF analysis revealed a white blood cell count of > 5000 cells/μL (> 60% polymorphonuclears), glucose level of 1.2 mmol/L, protein level of 2.17 g/L, and lactate level of 10.2 mmol/L.

The patient was diagnosed with bacterial meningitis, admitted to the intensive care unit, and started on third-generation cephalosporin (ceftriaxone 2 g q12h), vancomycin (15 mg/kg q12h), and ampicillin (2 g q4h).

C. koseri was detected in a CSF culture the following day, initially identified by matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF). Antimicrobial susceptibility testing, obtained using the BD Phoenix automated identification and susceptibility testing system, revealed *C. koseri* resistance to ampicillin, ampicillin-sulbactam, cefuroxime, ceftriaxone, and cefepime. However, it was susceptible to piperacillin-tazobactam, meropenem, gentamicin, ciprofloxacin, and trimethoprim-sulfamethoxazole. Due to concerns about hemodynamic instability and limited clinical improvement, antibiotics were changed to meropenem, 2 grams every 8 hours, based on susceptibility testing.

The patient's encephalitis and meningitis panel, along with blood cultures, were negative for other pathogens (HSV 1 and 2, VZV, CMV, HHV 6, enterovirus, *Cryptococcus spp.*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Neisseria meningitidis*, *Listeria monocytogenes*, and *Escherichia coli*). CSF-VDRL was also negative.

Magnetic resonance imaging (MRI) of the head revealed mucosal disease of the paranasal sinuses and loculated cystic areas in the sphenoidal sinus region with thick rim of enhancement and diffusion restriction suggesting infection. A focal area of loss of enhancement was seen in the roof of one of the cystic components at the floor of the sella. A small amount of fluid showing diffusion restriction in the dependent aspect of the occipital horns suggested pus, as shown in Figure 1. The patient was treated with an extended infusion of intravenous meropenem (2 g every 8 hours for three weeks) with adjunctive intrathecal meropenem and colistin for five days.

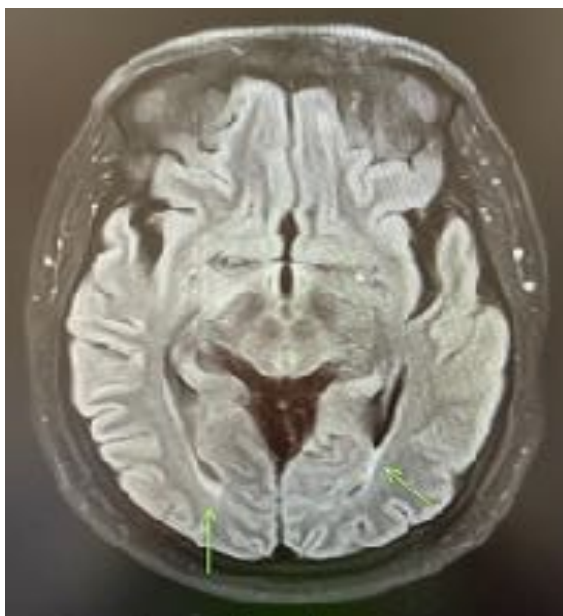


Figure 1: Focal area of loss of enhancement in the roof of one of the cystic components at the floor of the sella. A small amount of fluid showing diffusion restriction in the dependent aspect of the occipital horns, suggesting pus.

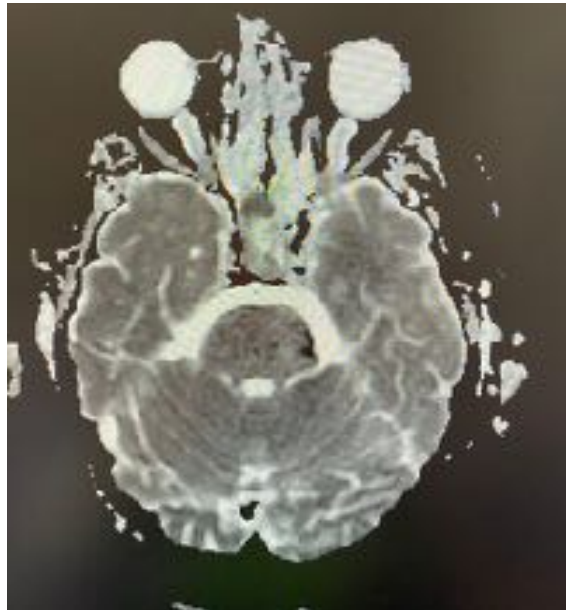


Figure 2: Follow-up brain MRI after completing 21 days of intravenous antibiotics showing resolution of fluid/pus in the occipital horns.

A lumbar drain was inserted to reduce CSF pressure. Subsequent CSF cultures were sterile including at the end of intrathecal therapy.

A few days after the initiation of antibiotic treatment, the patient's neurological status improved, and he became responsive and able to communicate. There was defervescence of fever. The lumbar drain was removed seven days after placement paralleled with the resolution of high opening pressure. A follow-up brain MRI after completing 21 days of IV antibiotics showed notable resolution of fluid/pus in the occipital horns [Figure 2]. Guided by the CSF profile [Table 1] and radiological data, intravenous meropenem was discontinued at three weeks. He was at his baseline neurologically upon discharge after a 19-day hospital stay.

Table 1: CSF analysis and gram stain.

Parameters	Lumbar Puncture – Day 1	Lumbar Puncture – Day 5
Appearance	Cloudy	Clear
Leukocytes	5420	200
Polymorphs	60%	25%
Lymphocytes	40%	75%
Erythrocytes	47	0
Gram stain	Gram-negative rod	Nil
Bacterial culture	<i>Citrobacter koseri</i>	No growth

Intrathecal meropenem (Archifar® Medochmie LTD, Cyprus) was administered at a dose of 20 mg every 12 hours, prepared in a sterile environment using aseptic technique.² One gram of meropenem was dissolved in 20 ml of sterile water, resulting in a concentration of 50 mg/ml. Then, 0.4 ml (20 mg) of this solution was further diluted in 0.6 ml of sterile saline to make a total of 1 ml for intrathecal administration. Similarly, colistin (Atlan Pharmaceuticals, S.A. Spain) was prepared for intrathecal administration at a dose of 125 000 international units once daily.^{3,4} One million units of colistin was dissolved in 10 ml of sterile water, 1.25 ml (125 000 IU) was taken for intrathecal administration. For intrathecal administration of antibiotics, the selected agent should always be free of preservatives and chelating agent⁵ and due to unavailability of preservatives/chelating free

aminoglycosides in our institute, their use was deferred and was replaced with colistin (Atlan Pharmaceuticals, S.A. Spain) and meropenem (Archifar® Medochmie LTD, Cyprus), both of which were ensured to be preservatives/chelating free.

Discussion

C. koseri is a gram-negative, rod-shaped, facultative anaerobic bacterium that belongs to the *Enterobacteriaceae* family.¹ It is commonly found in water, soil, and both human and animal digestive tracts. Despite its generally low virulence, *C. koseri* can cause various infections, including those of the intra-abdominal tract, urinary tract, respiratory system, skin and soft tissues, bones, blood stream, eyes, and central nervous system.⁶

Understanding the modes of transmission is crucial in preventing the spread of *C. koseri* meningitis and implementing effective infection control measures. In the hospital settings, transmission can occur through the use of contaminated medical equipment. Therefore, preventive measures such as proper hand hygiene, and sterile techniques during invasive procedures are crucial.

Table 2: Reported cases of *C. koseri* meningitis or ventriculitis in an adult patient.

Auth or / reference	Year of publication	Gender, age in years	Medical background	Risk factors	<i>C. koseri</i> susceptibility	Treatment	Surgical intervention	Outcome/complications
L. V. BOOTH et al. ⁷	1992	Female, 66	Type II diabetes mellitus	* <i>C. koseri</i> urinary infection associated with a staghorn calculus one month before presentation. *Spontaneous intracranial hemorrhage treated with an anterior communicating artery aneurysm clipping nine years before	Resistant Ampicillin.	Sensitive to Gentamicin, netilmicin, cotrimoxazole, cefotaxime, and ciprofloxacin	ventricular drain	Survived/ weakness and spasticity
Christophe et al. ⁸	2005	Female, 78	Ischemic heart disease, paroxysmal atrial fibrillation, and hypertension	*Ten days course of high-dose steroid treatment. *Meningioma.	Not available	Meropenem	Craniotomy	Survived/ mild cognitive deficits

Heng - Wei et al. ⁹	2015	Male, 73	Type II diabetes mellitus	*Urinary infection for one month before presentation.	Ampicill in	Cefazoli n, gentami cin, imipene m, ciproflo xacin, cefmetaz ole, ceftazidi me, aztreona m, ceftriaxo ne, cefepim e, levoflox acin, and meropen	ceftria xone	Craniot omy and surgica l drain	Survived/ complete recovery
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Cases of *C. koseri* meningitis or ventriculitis in adult patients are rare, with reported instances typically involving immunocompromised individuals. Unlike our case, all reported cases (given in Table 27⁹) were associated with some degree of immunosuppression, such as diabetes and steroid use, suggesting a potential association between *C. koseri* and immunosuppression, particularly in CNS involvement. Our patient, who was not diabetic or taking immunosuppressive medications, raises the likelihood of *C. koseri* causing meningitis in immunocompetent patients under the right circumstances.

Similarly to our case, one instance involved CNS surgical intervention years before presentation, suggesting a potential association between prior surgical interventions and *C. koseri* meningitis. This could be explained by changes in normal anatomy facilitating the entry of the organism to the brain, or the use of contaminated medical equipment during prior surgery introducing pathogenic organisms. This can increase the tendency to be infected with the same organism years after. Proceeding urinary tract infection caused by the same bacteria ahead of meningitis may further suggest the possibility of hematogenous seeding.

Although *C. koseri* is usually sensitive to most antibiotics, but it can acquire antimicrobial resistance through plasmid-mediated genes. Resistance to carbapenems in *C. koseri* has been reported at rates from 0 to 6.5%.¹ Our case showed extended-spectrum beta-lactamase production, emphasizing the importance of individual susceptibility testing.

Despite effective antibiotic therapy, bacterial meningitis remains a serious condition with a high fatality rate. Refractory intracranial hypertension with brain herniation and brainstem compression is the most common cause of mortality in these patients.¹⁰ The use of lumbar drainage in severe acute bacterial meningitis was demonstrated to be safe and feasible. In addition to antimicrobial therapy, the use of lumbar drain in admission to antimicrobial therapy was significantly associated with low morbidity and mortality.¹¹

Meningitis caused by *C. koseri* in neonates is associated with high rates of mortality (30%) and morbidity (50%).¹² Despite all reported cases surviving, survivors may suffer from long-term neurological sequelae, such as cognitive impairment, memory problems, and motor deficits, which was observed in one cases.^{7,12} For the same reason, it is important for healthcare providers to be aware of these potential complications and to provide appropriate follow-up care for patients who have recovered from the acute phase of the infection.

Ventriculitis is the inflammation of the ventricular fluid and the ependymal lining of the ventricles. Systemic antimicrobials based on the CSF culture results are the treatment for ventriculitis. However, the blood-brain barrier and blood-CSF barrier function as lipid layers in the CSF compartment, which may be a challenge in achieving therapeutic antimicrobial concentrations in the central nervous system via intravenous treatment alone. Intrathecal antibiotic treatment enables us to obtain the CSF concentration to the desired levels with a low potential for systemic toxicity. It allows direct access to the extracellular central nervous compartments by bypassing anatomical barriers, and high CSF drug levels can be attained with relatively small doses.¹³ Therefore

intraventricular antibiotic instillation can be used as an adjective therapy along with systemic antibiotics in patients with severe ventriculitis especially with difficult to treat organisms.¹⁴

Conclusion

Meningitis caused by *C. koseri* is an uncommon but serious in adults. The presence of previous CNS surgical intervention or immunocompromised status in a patient who presents with meningitis should raise suspicion for *C. koseri* as a possible cause. While *C. koseri* is usually susceptible to antibiotics, meropenem can be considered, especially if there is no improvement within the first 24 hours of treatment. The use of intrathecal antibiotics and lumbar drain as adjunctive therapy may contribute to patient survival.

Disclosure

The authors declared no conflicts of interest. Written consent was obtained from the patient.

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