

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

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Abstract

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 have a tendency to develop central nervous system abscesses. Meningitis caused by *C. koseri* in adults is extremely rare. Here we report a case of *C. koseri* meningitis in an immunocompetent adult post ENT procedure.

Case Report

A 48-year-old man was admitted to our hospital for torpid headache, fever, vomiting, and altered mental status. His symptoms started 7 days before. He had a recent history of undergoing nasal endoscopy indicated for rhinosinusitis. His past medical history was significant foressential hypertension and primary hypothyroidism, pituitary adenoma that was resected 2 years ago, and recurrent deep venous thrombosis.

On admission, body temperature was elevated at 38.0 C, the blood pressure 131/78 mm Hg, the heart rate 82 beats per minute, the respiratory rate 18 breaths per minute, and the oxygen saturation 96% while he was breathing ambient air. On neurologic examination, he was somnolent, and disorientated. He had nuchal rigidity, no skin petechiae were observed. No cranial nerve abnormalities were present.

Computed tomography (CT) of the brain was normal. Blood levels of glucose and electrolytes were normal, as were results of liver-function, kidney- function (UE), and coagulation tests. A laboratory examination revealed an elevated C-reactive protein level (337 mg/L) and a white blood cell count of (18,600/mm³).

Lumbar puncture (LP) was performed during the first hour of admission. The macroscopic appearance of the CSF was purulent an elevated opening pressure (50 mmH₂O). White blood cell count: >5000 cells/_L (>60% polymorphonuclears), glucose level: 1.2 mmol/L, protein level: 2.17 g/L, lactate level: 10.2 mmol/L.

The diagnosis of bacterial meningitis was established, the patient was admitted to the ICU and was started on third-generation cephalosporine (Ceftriaxone 2 g q12h), Vancomycin 15 mg/kg q12h, and ampicillin 2 grams q4h.

The day following admission, *Citrobacter koseri* was detected in a bacterial culture of the CSF sample. It was initially identified by matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF). Then, antimicrobial susceptibility testing was obtained using BD Phoenix automated identification and susceptibility testing system. *C. koseri* was resistant to Ampicillin, Ampicillin-Sulbactam, Cefuroxime, Ceftriaxone, and Cefepime. However, it was susceptible to Piperacillin-Tazobactam, Meropenem, Gentamicin, Ciprofloxacin, and

Trimethoprim-Sulfamethoxazole. Later in the day and due to concerns of hemodynamic instability and limited clinical improvement, antibiotics were changed to Meropenem 2 grams q8h. The organism was non-cephalosporin susceptible however sensitive to aminoglycosides and Meropenem, as per the susceptibility profile resulted on hospital day 3.

The patient’s encephalitis and meningitis panel, which tested for HSV 1 and 2, VZV, CMV, HHV 6, enterovirus, *Cryptococcus spp.*, *S. pneumoniae*, *H. influenzae*, *N. meningitides*, *L. monocytogenes*, and *E. coli*, were all negative. CSF VDRL was also negative. His preliminary blood cultures showed no growth.

Magnetic resonance imaging (MRI) of the head revealed significant mucosal disease of the paranasal sinuses. Loculated cystic areas in the region of the sphenoidal sinus with thick rim of enhancement and diffusion restriction suggesting infection. Focal area of loss of enhancement in the roof of one of the cystic components at the floor of the sella. Small amount of fluid showing diffusion restriction in the dependent aspect of the occipital horns suggesting pus as shown in [Figure 1]. As a result, he was treated with extended infusion of intravenous meropenem 2 g every 8 hours for 3 weeks with adjunctive intrathecal meropenem and colistin for 5 days.

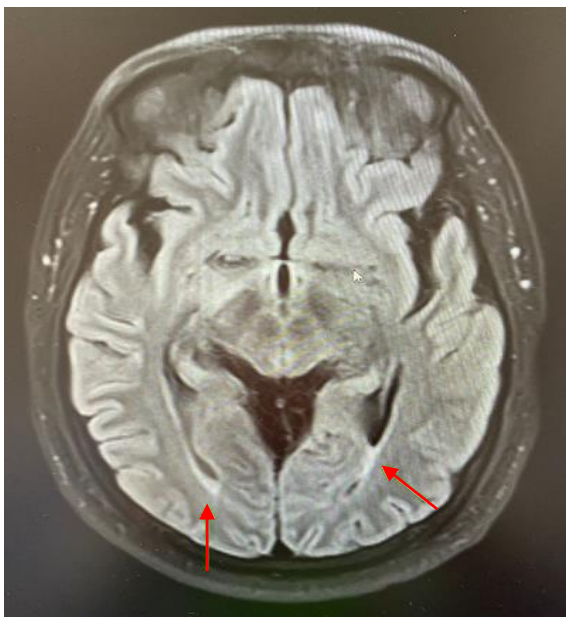


Figure 1: Focal area of loss of enhancement in the roof of one of the cystic components at the floor of the sella. Small amount of fluid showing diffusion restriction in the dependent aspect of the occipital horns suggesting pus

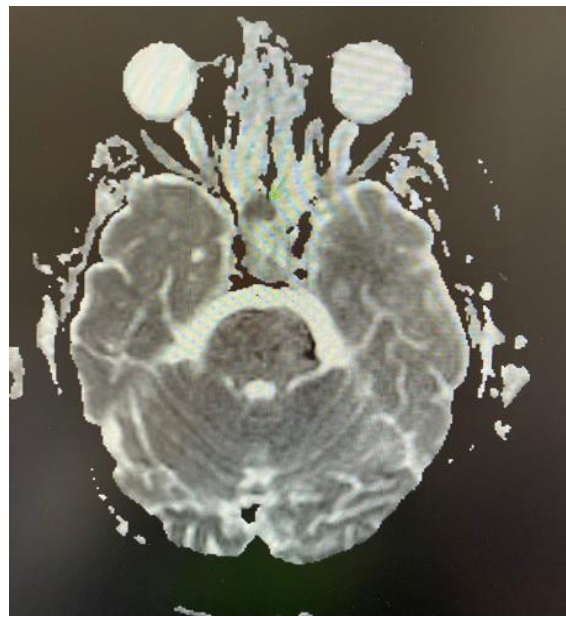


Figure 2: follow up MRI brain after completing 21 days of IV antibiotics showed was notable for resolution fluid/pus in the occipital horns.

A lumbar drain was inserted to reduce CSF pressure. CSF cultures were collected at the time of lumbar drain placement and returned negative. Three subsequent CSF cultures were found to be sterile including at the end of intrathecal therapy.

A few days after the initiation of antibiotic treatment, the neurological status improved, and the patient was responsive and able to communicate. There was defervescence of fever. The lumbar drain was removed 7 days after placement paralleled with resolution of high opening pressure. A follow up MRI brain after completing 21 days of IV antibiotics showed was notable for resolution fluid/pus in the occipital horns as shown in [Figure 2]. Guided by CSF profile [Table 1] and radiological data, intravenous Meropenem was discontinued at 3 weeks. He was at his baseline neurologically when discharged 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

Meropenem (Archifar® Medochmie LTD, Cyprus) was administered to the patient through intrathecal route with dose of 20 mg every 12 hours intrathecally which was prepared in a sterile environment using aseptic technique.¹ 1 gram of Meropenem was dissolved in 20ml of sterile water, resulting in a concentration of 50mg/ml of Meropenem. Then 0.4ml (20mg) of this solution was further diluted in 0.6ml of sterile saline to make a total of 1ml for intrathecal administration. In the same aseptic manner, colistin (Atlan Pharmaceuticals, S.A. Spain) was prepared for intrathecal administration. The dose of Intrathecal colistin was 125,000international units once a day.^{2,3} 1 million units of colistin was dissolved in 10ml of sterile water, 1.25ml (125,000IU) was taken from this prepared solution for intrathecal administration. For intrathecal administration of antibiotics, the selected agent should always be free of preservatives and chelating agent⁴ 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) in addition to Meropenem (Archifar® Medochmie LTD, Cyprus), both of which were ensured to be preservatives/chelating free.

Discussion

Citrobacter koseri is a gram-negative, rod-shaped, facultative anaerobic bacterium that belongs to the *Enterobacteriaceae* family.⁵ It is commonly found in water, soil, and both human and animal digestive tracts. Despite being generally thought of as having low virulence, *C. koseri* may cause a variety of 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 various modes of transmission is important 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 in reducing the incidence of *C. koseri* meningitis.

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

Author / reference	Year of publication	Gender, age in years	Medical background	Risk factors	<i>C. koseri</i> susceptibility		Treatment	Surgical intervention	Outcome / complications
					Resistant	Sensitive			
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 presentation.	Ampicillin.	Gentamicin, netilmicin, cotrimoxazole, cefotaxime, and ciprofloxacin	Netilmicin and cefotaxime	ventricular drain	Survived / weakness and spasticity

Christopher 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.	Ampicillin	Cefazolin, gentamicin, imipenem, ciprofloxacin, cefmetazole, ceftazidime, aztreonam, ceftriaxone, cefepime, levofloxacin, and meropenem.	ceftriaxone	Craniotomy and surgical drain	Survived / complete recovery

C. koseri meningitis or ventriculitis in an adult patient was only reported in three cases as demonstrated in [Table 2].⁷⁻⁹ Unlike our case, all reported cases were considered immunocompromised to some extent in view of diabetes and steroids. This demonstrates the possible association between *C. koseri* and immunosuppression which increases the probability of being infected with this organism especially central nervous system (CNS) involvement. However, our patient was not diabetic or received immunosuppressive medications which raises the likelihood of *C. koseri* causing meningitis in immunocompetent patients as well under the right circumstances.

Similar to our patient, one case had CNS surgical intervention years before presentation. This can raise the potential association between previous CNS surgical intervention and *C. koseri* meningitis which might be explained by change in the normal anatomy that may ease the entry of organism to the brain in the future. Another explanation is that prior surgical intervention may also contribute by changing the normal flora through the usage of contaminated medical equipment which may introducing new pathogenic organisms such as *C. koseri*. 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, however it can acquire antimicrobial resistance through plasmid-mediated genes. Resistance to carbapenems was observed to range from 0 to 6.5% in *C. koseri*.⁵ In contrast to reported cases where *C. koseri* was sensitive, *C. koseri* isolated from our patient was extended-spectrum b-lactamase-producer.

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 addition to antimicrobial therapy was a 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 In spite of all reported cases have survived, survivors may suffer from long-term neurological sequelae, such as cognitive impairment, memory problems, and motor deficits which was observed in one of the cases.^{7,12} For 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 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 adjuvant 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 infection in adults. The presence of previous CNS surgical intervention or immunocompromised status in a patient who presents with meningitis should raise the suspicion for *C. koseri* as a possible cause. Despite it is usually a susceptible organism, meropenem can be considered for *C. koseri* treatment especially if there is no improvement in the first 24 hours of treatment. The use of intrathecal antibiotics and lumbar drain as adjuvant therapy may contribute to the patient survival.

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