Elizabethkingia meningoseptica—An Emerging Cause of Neonatal Meningitis
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Abstract
Elizabethkingia meningoseptica is a multidrug-resistant organism that causes human infection, rarely. However, it may get colonized in the hospital environment and can cause healthcare-associated infections. Infections caused by E meningoseptica are difficult to treat because of intrinsic resistance of this bacterium to multiple antibiotics. We report herewith a case of E meningoseptica meningitis with sepsis in a term neonate who developed hydrocephalus as a complication and was successfully treated with multiple antibiotics (IV cefoperazone + sulbactam, ciprofloxacin, and oral cotrimoxazole and rifampicin).

Key Words: Elizabethkingia meningoseptica, neonatal meningitis, neonatal sepsis, hydrocephalus, minocycline, fluoroquinolones, rifampicin

Background
Elizabethkingia meningoseptica is a ubiquitous gram-negative bacillus, typically isolated from plants, soil, and water, including chlorinated water, and may colonize the hospital environment, particularly tap water and sinks. It is not considered a part of the normal human microflora.1,2 Originally described by the American bacteriologist Elizabeth O King as Flavobacterium meningoseptica in 1959 and reclassified as Chryseobacterium meningoseptica in 1994, it was assigned the genus Elizabethkingia under the family Flavobacteriaceae in 2005, based on 16s rRNA phylogenetic studies.2 Individual cases of meningitis and
sepsis as well as outbreaks caused by *E meningoseptica* have been reported in preterm and low-birthweight neonates; however, this microorganism rarely causes infection in immunocompetent individuals.\(^1\) *E meningoseptica* infections carry high morbidity and mortality rates and are associated with serious postinfectious sequelae, including hydrocephalus, deafness, and developmental delay.\(^1\)\(^3\) We report a case of complicated *E meningoseptica* infection in a full-term neonate. It was successfully treated with combination chemotherapy.

**Case Presentation**

A full-term male neonate was transferred to the NICU because of severe meconium aspiration syndrome on day 2 of life. The neonate exhibited respiratory distress, and required mechanical ventilation and surfactant therapy. Inotropic support (dopamine and milrinone) was required to manage associated shock and pulmonary hypertension. The neonate was weaned on heated humidified high-flow nasal cannula support on day 5 of life. He was started on first-line antibiotics (ampicillin and gentamicin) at admission after collecting blood sample. The blood sample was found to be sterile and IV antibiotics were discontinued on day 5. The neonate developed an episode of fever with erythematous rash all over the abdomen on day 5 within 6 hours of stopping antibiotics. Sepsis screen was positive (C-reactive protein, 10.8 mg/L and procalcitonin, 6.2 ng/mL). Blood and cerebrospinal fluid (CSF) samples were collected for culture test, and the neonate was started on IV piperacillin + tazobactam for managing suspected sepsis. CSF culture was cloudy with 8000 cells/µL (90% neutrophils and 10% lymphocytes), and he had elevated protein level (760 mg/dL) and decreased CSF glucose level (10 mg/dL). The blood culture showed gram-negative bacilli on blood agar (Figure 1) and chocolate agar (Figure 2). There was no growth on MacConkey agar. The colonies on blood agar were pale yellow with grayish discoloration at the periphery. The bacilli were oxidase positive and were identified as *Elizabethkingia meningoseptica* by Vitek 2 (Biomerieux, Marcy l’Etoile, France). This isolated organism was multidrug resistant. It was resistant to piperacillin + tazobactam, carbapenems, aminoglycosides, and vancomycin, but sensitive to cefoperazone + sulbactam and fluoroquinolones. Antibiotics were modified as per sensitivity pattern, and the neonate was started on cefoperazone + sulbactam (in 1:2 ratio) along with ciprofloxacin. The same organism was found in CSF culture also, with similar sensitivity pattern. The neonate continued to have, daily, 2 episodes of fever with rash despite...
Masrani KM, et al. Elizabethkingia meningoseptica

Case Report

being on sensitive antibiotics. The CSF examination after 1 week of IV antibiotics showed the presence of 5400 cells/µL, with 95% neutrophils and 540 mg/dL protein. CSF culture again grew the same organism. Manual sensitivity of the organism revealed additional sensitivity to rifampicin and cotrimoxazole, which were then added to the existing antibiotic regimen. The neonate became afebrile after 5 days of oral antibiotics, and rash also disappeared. A repeat CSF culture after 7 days of oral rifampicin and cotrimoxazole and 14 days of IV antibiotics was sterile and showed a reduction in cellular count (3100 cells/µL with 90% neutrophils). However, there was a persistent rise in protein level to 400 mg/dL. The neonate developed convulsions during this period and required anticonvulsant therapy with phenobarbitone and levetiracetam. The neonate's head circumference showed disproportionate growth, which was later confirmed on neurosonogram to be due to the development of communicating hydrocephalus. The neonate required CSF reservoir placement for rapidly increasing ventricular size to facilitate repeated CSF tapping to control the accelerated increase in ventricular size. Then, the CSF showed progressive clearing; and after 3 weeks of IV antibiotics and 2 weeks of oral antibiotics, CSF showed 46 cells/µL with 15% neutrophils and protein level at 199 mg/dL. The neonate was discharged home on oral antibiotics (rifampicin and cotrimoxazole for 3 more weeks, total 6 weeks of antibiotics for meningitis with ventriculitis). Periodic CSF reservoir tapping was performed, on OPD basis, to avoid excessive increase in ventricles’ size. By the end of the treatment, the CSF culture was again documented to be sterile with normal protein level (total 3 documented sterile cultures). The neonate was enrolled for a neurodevelopment follow-up program. He also required ventriculoperitoneal shunt placement on follow-up for increasing ventricular size despite repeated reservoir tapping. At 4-month follow-up, the neonate was found to be developmentally normal for age.

Discussion

E meningoseptica infection is associated with a high mortality rate (as high as 30%) because of lack of effective therapeutic regimens, antibiotic resistance, and virulence. As this is an emerging drug-resistant pathogen of the NICU, standard guidelines about antibiotic of choice or consensus about combination chemotherapy or duration of therapy are lacking. The most reported outbreaks involve a handful of cases of either preterm or low-birth-weight neonates after prolonged mechanical ventilation or hospital stay. However, earlier infections (median duration: 3–7 d) were also reported. Tai et al reported an outbreak of E meningoseptica sepsis in 3 term neonates due to environmental contamination by a pacifier box.

E meningoseptica is the only microorganism reported to possess 2 chromosomally encoded metallo-b-lactamase (MBL) genes responsible for carbapenem resistance. Though a gram-negative bacillus, E meningoseptica is highly sensitive to antibiotics such as vancomycin, rifampicin, piperacillin–tazobactam, newer fluoroquinolones, minocycline, and, possibly, tigecycline, which are used to treat gram-positive infections. The efficacy of vancomycin monotherapy is reduced because of drug resistance. High mortality in vancomycin monotherapy group is mainly because only about 20% of E meningoseptica isolates, in a study, showed intermediate susceptibility to vancomycin in vitro and the rest being resistant. Minocycline, the newer fluoroquinolone, and rifampicin were the most effective drugs with more than 90% and 88% susceptibility, respectively. The Clinical Laboratory Standards Institute standard does not define a breakpoint for vancomycin for E meningoseptica and hence, the exact MIC cannot be defined. An in vitro sensitivity in laboratory does not always mean that the antibiotic works in the index case in real-life situation and results in clinical cure. Hence, a multidrug combination therapy is supposed to be more effective; and addition of ciprofloxacin, linezolid,
or rifampicin is necessary to treat *E meningoseptica* infection effectively.10-12

**Conclusion**

This case report highlights the effective management of *E meningoseptica* meningitis and suspected ventriculitis with a combination of IV and oral antibiotics.

**References**


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