Section: Neonatology

Original Research Article

CLINICAL PROFILE OF ELIZABETHKINGIA MENINGOSEPTICA IN NEWBORNS: INSIGHTS FROM A TERTIARY LEVEL NEONATAL INTENSIVE CARE UNIT IN NORTH KERALA

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ABSTRACT

Elizabethkingia species are known to cause potentially fatal infections in newborns. We present our experience in treating six infants with Elizabethkingia meningoseptica sepsis, including both term and preterm infants. In all cases, Elizabethkingia meningoseptica was found in either the blood or cerebrospinal fluid cultures. Prompt and appropriate use of antibiotic combinations, along with supportive care, resulted in significant recovery and curability in most of our patients.

Keywords: Elizabethkingia meningoseptica, meningitis, bacteremia, antibiotics.

INTRODUCTION

Elizabethkingia meningoseptica, previously known as Flavobacterium meningosepticum, is a rod-shaped gram-negative bacterium widely distributed in nature (e.g., in water, plants and soil). Many environmental studies have shown that E. meningoseptica can survive in chlorine-treated municipal water supplies, often colonizing sink basins and taps, and has become a potential reservoir for infections in the hospital environment. The organisms have been recovered from dialysis systems, pharmaceuticals, and medical devices (including intravascular catheters, respirators, and intubation tubes).[1,2] Common diagnoses associated with Elizabethkingia species include pneumonia, urinary tract infections, meningitis, and bacteremia, with other unusual presentations such as septic arthritis, peritonitis, and abscesses.[3,4] Elderly, newborns, and immunocompromised patients are most susceptible to this infection, with recorded case-fatality rates of over 50%.[5] Its intrinsic resistance and recent reports of multi-drug resistant strains are a cause for growing concern. In the absence of established guidelines for antibiotic susceptibility testing and lack of evidence-based treatment regimens, treatment failures are common with poor patient outcomes.[6]

In this case series, we report 6 cases involving Elizabethkingia meningoseptica bacteremia in newborns admitted to a tertiary care hospital. These cases highlight the clinical challenges and potential complications associated with Elizabethkingia infections in neonates.

Ethical Approval and Informed Consent

Informed consents were obtained from the patients' caretaker for the publication of this case series.

Case 1

A male infant (39 w+ 2 d) weighing 3.6 kg, was delivered via emergency cesarean section due to cord prolapse and meconium-stained amniotic fluid. The baby had perinatal asphyxia and required intubation and therapeutic hypothermia. Central lines were accessed. He was started on an Injection of Ampicillin.CBC was normal. The CRP level was 17.3 mg/L, and the blood culture taken at admission was negative. On the sixth day of life, he developed

multiple episodes of hypoglycemia and one seizure episode. A sepsis workup was repeated, revealing a CRP level of 82.8 mg/L while the complete blood counts remained normal. CSF analysis was suggestive of meningitis (TLC 470 cells/cumm, N 30%, L 70%, glucose 26 mg/dl, protein 73.5 mg/dl). Antibiotics were changed to Meropenem and Vancomycin. Both blood and CSF cultures yielded Elizabethkingia meningoseptica. Antibiotics were adjusted according to the sensitivity pattern which included Levofloxacin, Cefoperazone Sulbactam, and Cotrimoxazole. Hypoglycemia and seizures were controlled, but he developed fever spikes. CSF analysis was repeated at regular intervals to monitor the response, showing leukocytosis with hypoglycorrhachia (lowest glucose 4 mg/dL) and elevated protein levels (highest protein 359 mg/dL). Minocycline was added, resulting in the resolution of the fever. Follow-up blood and CSF cultures continued to show no growth. An MRI of the brain revealed patchy meningeal enhancement in the left frontal and temporal areas, a subdural collection affecting both frontal convexities, with no signs of ventriculitis or cerebral abscesses (fig 1). The subdural collection was drained, and the culture of the aspirate was negative. After a six-week course of appropriate antibiotics, both the MRI of the brain and CSF analysis were repeated, indicating improvement. Intravenous antibiotics were discontinued, and the infant was discharged home with a two-week course of oral antibiotics (Levofloxacin and Cotrimoxazole). Currently, he is six months old with age-appropriate developmental milestones.

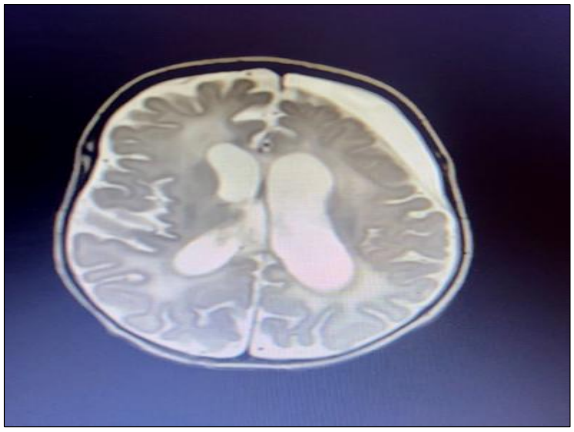

Figure 1: T2 axial image showing subdural hemorrhage in bilateral frontal convexities(L>R) with bilateral mild ventriculomegaly

Case 2

A male infant (26 w + 2 d) weighing 850 grams, was delivered vaginally from a twin pregnancy. The baby was intubated at birth required surfactant, mechanical ventilation, IV antibiotics and was subsequently placed on CPAP. Central lines were placed. On the seventh day of life, he developed hyperglycemia and feed intolerance, prompting the initiation of antibiotics (Piperacillin Tazobactam and Amikacin). A Sepsis screen showed leukocytosis, while CRP was 70 mg/L. The baby had seizures and episodes of apnea, leading to reintubation. Blood cultures revealed Enterobacter species. Antibiotic therapy was adjusted based on the sensitivity results (Meropenem and Amikacin). CSF analysis suggested meningitis, with the CSF culture confirming Elizabethkingia meningoseptica. Neurosonography revealed an infective collection in the subarachnoid space, accompanied by ventriculomegaly. The infant's condition continued to worsen with recurring seizures, prompting a change in antibiotics according to the sensitivity of Elizabethkingia meningoseptica (Vancomycin, Levofloxacin, Meropenem, and Minocycline). Follow-up blood cultures indicated the growth of Acinetobacter species. The frequency of seizures diminished, and CRP levels showed a decreasing trend. The infant was extubated to CPAP support, and subsequent blood and CSF cultures were sterile. The baby developed post-meningitic hydrocephalus (fig 2) for which serial lumbar puncture was done. Later, a ventriculosubgaleal shunt was placed which was then revised with a ventriculoperitoneal shunt. On follow-up, the baby was noted to have a gross motor delay.

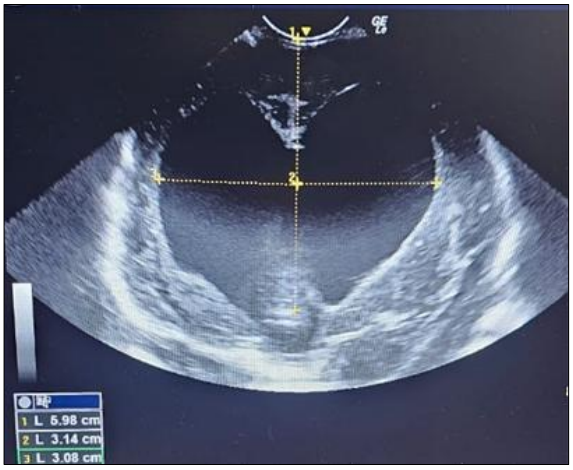

Figure 2: Neurosonogram demonstrating ventriculomegaly with left-side Levene index 31.4 mm and right-side index 30.8 mm

Case 3

A male infant (27 w + 5 d) weighing 1.015 kg was delivered via emergency cesarean section. Shortly after birth, he developed respiratory distress requiring surfactant administration and IV antibiotics. Central lines were placed. On the 13th day of life, on CPAP, the infant developed multiple episodes of apnea, tachycardia, and shock. He was placed on mechanical ventilation. Inotropes along with Piperacillin Tazobactam and Amikacin were started. Echo ruled out hemodynamically significant PDA. A complete blood count indicated leukocytosis (29,910 cells/cumm), and CRP was elevated at 113 mg/L. Antibiotics were changed to Meropenem, Vancomycin, and Colistin. Lumbar puncture was initially deferred due to hemodynamic instability. By day 14, the baby had seizures that necessitated multiple anticonvulsant medications. CRP showed an

increasing trend of 150 mg/L. CSF analysis suggested meningitis (TLC-753 cells/cumm N-52%, L-48%, glucose 3mg/dl, protein 386.1mg/dl) and blood cultures yielded Elizabethkingia meningoseptica. Antibiotics were changed to Cefoperazone + Sulbactam and Ciprofloxacin. A neurosonogram revealed a grade 4 intraventricular hemorrhage on the left side. Serial CRP measurements indicated a decreasing trend and follow-up blood cultures were sterile. CSF culture remained sterile throughout. Antibiotics were continued for 21 days. The baby developed hydrocephalus for which serial CSF tapping was done. Later, a ventriculoperitoneal shunt was placed. Currently, the baby is one-year-old with global developmental delay.

Case 4

A term (37 w + 6 d) male infant, 2 days old with a birth weight of 2.66 kg, delivered via spontaneous vaginal delivery was subsequently referred to our facility due to multiple episodes of hypoglycemia within the first 48 hours. Upon examination, the infant was hemodynamically stable and exhibited moderate activity. Hypoglycemia was addressed with intravenous fluids. A complete blood count indicated mild thrombocytopenia (126 x 10^3/µL), and CRP was 79.97 mg/L. The coagulation profile was normal. Piperacillin Tazobactam and Amikacin were initiated. CSF analysis revealed hypoglycorrhachia, prompting a change in antibiotics to Meropenem and Amikacin. Blood cultures taken on the day of admission identified Elizabethkingia meningoseptica. Serial CRP tests indicated a decreasing trend and follow-up blood cultures returned sterile results. CSF culture was sterile. Intravenous antibiotics were administered for 21 days, during which the infant demonstrated clinical improvement. An MRI of the brain revealed several periventricular hemorrhagic foci, along with small scattered foci of subdural and subpial hemorrhage in both cerebellar hemispheres and the left frontal lobe which we couldn't attribute to any specific cause. On follow-up, the baby is thriving well with the attainment of milestones at the appropriate age.

Case 5

A male infant (28 w + 2 d) weighing 1.090 kg, was delivered via spontaneous vaginal delivery and referred to our facility 56 hours after birth. Shortly after birth, the infant developed respiratory distress requiring surfactant and IV antibiotics (Inj Piperacillin Tazobactam and Amikacin) and hemodynamically significant PDA requiring paracetamol. Upon admission, the infant was hemodynamically stable and maintained adequate oxygen saturation with a low-flow nasal cannula. Central lines were in place. On the eleventh day of life, the neonate experienced multiple apneic episodes and tachycardia, with CBC indicating a total leukocyte count of 26,800 cells/cumm and an elevated CRP level of 24.3 mg/L. Injection Piperacillin Tazobactam and Amikacin were reinitiated, and blood cultures revealed Elizabethkingia meningoseptica. Antibiotics were changed to Ciprofloxacin and Cefoperazone + Sulbactam. CSF analysis returned normal results, and serial CRP levels showed a decreasing trend. Follow-up blood cultures were sterile, and IV antibiotics were administered for an additional ten days. The infant was discharged home at 34 weeks of postmenstrual age. Currently, the baby is five and a half years old with age-appropriate developmental milestones.

Case 6

A male infant (25 w) weighing 765 grams was delivered vaginally. Soon after birth, the baby was intubated and surfactant was administered. Central lines were placed. Mother had suspected chorioamnionitis. Injection Piperacillin Tazobactam, Ampicillin, and Amikacin were started. At 12 hours of life, the baby developed hypotension. Hyperglycemia and sclerema were also observed. CBC showed leucocytosis (52,800 cells/cumm). CRP was normal. Serial CBC showed leukocytosis and thrombocytopenia. Antibiotics were escalated to Meropenem and Vancomycin. Initial blood cultures showed no growth. Inotropes were stopped by day 4 and the infant remained on mechanical ventilation with minimal ventilatory settings. On day 17, the infant's condition deteriorated, with an increased FiO2 requirement, elevated lactate levels in blood gas, and hypotension. The CBC reflected leukocytosis (30,460 cells/cumm) and thrombocytopenia (13,000 cells/µL), and CRP levels were elevated at 182 mg/L. Blood culture identified Elizabethkingia meningoseptica, Antibiotics were changed to Levofloxacin and Cefoperazone +Sulbactam. A lumbar puncture was deferred due to the infant's hemodynamic instability. Neurosonography and abdominal ultrasound revealed developing cerebellar abscesses and focal hepatic abscesses along with renal injury. A follow-up blood culture showed no growth. He wascontinued on mechanical ventilation with increased FiO2 requirement. Nonetheless, the infant's overall condition continued to deteriorate, leading to death on day 45.

Clinical profile of above cases summarised

Serial no	Gestational age	Birth weight (gms)	Inborn/ Outborn	Day of symptom	Culture proven Meningitis	Choice of antibiotics	Complication	Follow up
1	39w + 2d	3600	Inborn	Day 5	Yes	Cefoperazone+Sulbactam,Levofloxacin,Cotrimoxazole,Minocycline	Subdural collection	Normal

2	26w +2d	850	Inborn	Day 7	Yes	Vancomycin,Levofloxacin,Meropenem,Minocycline	Hydrocephalus	Gross motor delay
3	27w +5d	1015	Inborn	Day 13	No	Cefoperazone +sulbactam,Ciprofloxacin	Hydrocephalus	Global developmental delay
4	37w +6d	2660	Outborn	24 hours	No	Meropenem,Amikacin	No	Normal
5	28w+2d	1090	Outborn	Day 11	No	Cefoperazone +Sulbactam,ciprofloxacin	No	Normal
6	25w	765	Outborn	Day 17	No	Cefoperazon +sulbactam,Levofloxin	Cerebellar and hepatic abscess,death	-

DISCUSSION

E. meningoseptica is commonly found in the environment. In the literature, the majority of documented cases of infections linked to this organism are acquired in hospitals and frequently noted in immunocompromised individuals. Several cases of E. meningoseptica infection have been reported as part of outbreaks, and the source identified as contaminated hospital water supplies, saline, disinfectants, antibiotic solutions, water sinks, and respirators.[7,8] In our cases, the infection was thought to be of nosocomial origin. Predisposing factors in neonates include prematurity, very low birth weight, central venous catheters, immunosuppression, and prolonged and prior exposure to higher antibiotic concentrations.[9,10] Among our cases, 67% were born prematurely, 83% of patients had central lines in place when sepsis developed. Additionally, 67% of our cases had previously received broad-spectrum antibiotics for five days.

Our case 4 is distinctive in that the patient was infected with E. meningoseptica, and symptoms manifested within the first two days of life. In a case report by Wang et al., a baby presented with early onset Elizabethkingia sepsis.[11] In the sixth case, the development of multiple abscesses could result from the hematogenous dissemination of Elizabethkingia. While involvement of the liver is uncommon, instances of multi-organ abscesses have been documented.[12] Elizabethkingia meningoseptica is an uncommon cause of meningitis in newborns, mainly affecting those who are premature. Thong et al. documented a case series involving 7 neonates with meningitis due to Elizabethkingia meningoseptica, noting that over 50% had a low birth weight.[13] All the neonates exhibited symptoms during the first week of life, with 28.2% succumbing to the illness and 40% of the survivors developing hydrocephalus. We had two confirmed cases of Elizabethkingia meningitis through CSF culture both complicated with hydrocephalus.

Elizabethkingia meningoseptica is notable for its inherent resistance to several classes of antibiotics, including aminoglycosides, colistin, and most beta-lactams, such as carbapenems.[14] This intrinsic resistance poses significant challenges in managing infections caused by this organism. In our study, we identified the isolates (Fig 3) and determined their antimicrobial susceptibility using the VITEK 2 system (Biomerieux). The results were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) guidelines, and we adjusted our antibiotic choices based on the sensitivity patterns observed.

In our findings, 83.3% of the isolates were sensitive to Cefoperazone Sulbactam and Minocycline, while 50% showed sensitivity to Cotrimoxazole. A case report by Chammala SK et al. documented the successful treatment of a patient with Cefoperazone Sulbactam.[15] Additionally, research conducted by Raghad T. Alhuthil et al. indicated that Minocycline and trimethoprim/sulfamethoxazole demonstrated the greatest effectiveness, highlighting their potential role in treating E. meningoseptica infections.[16]

The latest studies demonstrated the benefit of fluoroquinolone, which can be explained by the superior pharmacokinetics as compared to hydrophilic antimicrobials, such as beta-lactams.[17] The fluoroquinolones are lipophilic agents, with better penetration through the blood-brain barrier, and are not as significantly affected by the variation of volume distribution during sepsis.[17,18] In all our cases, the isolates were sensitive to fluoroquinolones. In 83.3% of our cases, fluoroquinolones were used in combination with other antibiotic therapies.

Vancomycin has been suggested for the treatment of meningitis caused by Elizabethkingia meningoseptica, according to a study of medical literature. However, a number of recent investigations have questioned the effectiveness of this treatment due to the high minimum inhibitory concentration.[19,20] Additionally, successful use of Piperacillin/tazobactam has also been documented.[19]

E. meningoseptica infections present significant challenges for clinicians. Infections caused by this organism can be life-threatening if not identified and treated promptly. Infection control practices are crucial in the prevention of E. meningoseptica infections. The bacteria are well known for biofilm formation. In some cases, gentler approaches like the application of alcoholic hand sanitizer, using sterile water instead of tap water for baby care, fixing and disinfecting hospital water tanks, replacing sink

faucets, and flushing pipelines effectively reduced the infection.[21,22] Furthermore, periodic surveillance and continuous training programs are essential to reinforce the significance of hand hygiene and adherence to contact precautions among hospital staff.[23,24]

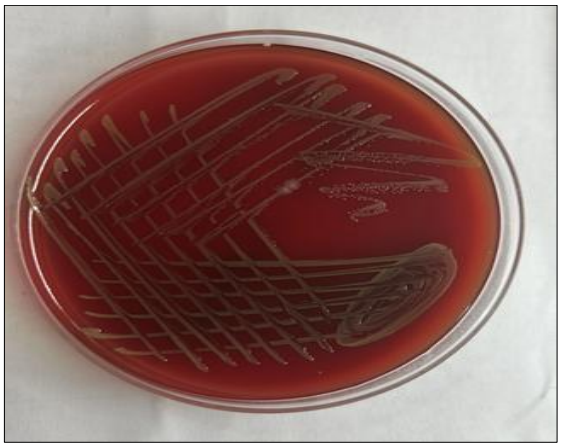

Figure 3: Blood agar showing colonies of Elizabethkingia meningoseptica

CONCLUSION

In both term and preterm newborns, Elizabethkingia species should be considered as a potential source of infection when there is no positive response to standard broad-spectrum antibiotics. Effective treatment includes antibiotics such as Cefoperazone Sulbactam, Vancomycin, Trimethoprim-Sulfamethoxazole, Minocycline, and Fluoroquinolones, also the removal of infection sources. Implementing infection control strategies is vital to prevent the spread of this bacterium. In our experience, prematurity and meningitis had poor outcomes.

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Consent for Publication

Consent for the publication of the clinical information and/or images was taken from the parents of the patients

Declaration of Conflicting Interests

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