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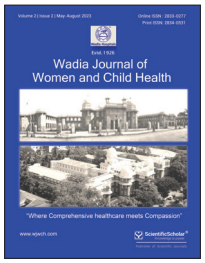

Case Report

Elizabethkingia meningoseptica: Changing anti microbial resistance causing fatal community-acquired neonatal meningitis – An area of rising concern

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ABSTRACT

Elizabethkingia meningoseptica is often reported as a hospital-acquired infection. We present an unusual fatal case of community-acquired meningitis probably secondary to contamination of the breast pump and feeding bottle used at home. Despite being a Gram-negative bacillus, it is extremely sensitive to antibiotics used to treat Gram-positive infections. There is a lack of protocolized effective treatment regimens and the organism demonstrates *in vitro* resistance to many antibiotics but a changing pattern of resistance as seen in our case is not reported till date. *E. meningoseptica* is an emerging potential source of neonatal infection and is an upcoming public health problem.

Keywords: *Elizabethkingia meningoseptica*, Neonatal meningitis, Community-acquired, Public health

INTRODUCTION

Elizabethkingia meningoseptica is a unique saprophytic Gram-negative bacillus. This organism is known for causing outbreaks among preterm hospitalized neonates in the neonatal intensive care unit (NICU). We present an unusual fatal case of community-acquired meningitis probably secondary to contamination of the breast pump and feeding bottle used at home, presenting with changing antibiotic resistance patterns leading to septicemia, meningitis, and neonatal encephalopathy.

CASE REPORT

A 33-year-old female primigravida conceived with *in vitro* fertilization, delivered through lower segment cesarean section due to failure of labor induction, a female neonate at term gestation with a birth weight of 2188 g. Antenatal ultrasound and Doppler scan were normal. Neonate had APGAR scores of 9 at both 1 and 5 min, and no resuscitation was required. She was kept in the postnatal ward and was discharged home on day 4 of life. At home, the neonate was started on bottle feeds with the mother's milk expressed using a manual breast pump. She was noted to have increasing irritability and poor oral intake for 2 days before admission. On day 14 of life, she was brought to our NICU for further management of persistent fever and poor feeding, At the time of

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admission vitals were heart rate (HR) – 168 bpm, respiratory rate (RR) – 58 pm, and Spo_2 – 98% suggestive of fever and associated tachycardia. Her blood sugar was normal. There was no evidence of shock or dehydration. Anthropometry as per modified Fenton's chart showed weight: 2392 g (< 3rd centile), head circumference (HC): 32 cm (10th–50th centile), and length 46 cm (50th–90th centile). She was irritable with full anterior fontanelle measuring 3 cm × 2.5 cm with palpable posterior fontanelle. Cranial nerves were normal. There was axial and appendicular hypertonia with hyperreflexia. Appendicular power was also reduced. Neonatal reflexes including sucking, rooting, and Moro reflex were reduced. There was no evidence of any neurocutaneous markers, no hepatosplenomegaly and rest of the examination was normal.

In view of suspected meningitis with septicemia, further workup revealed hemoglobin of 15.8 g%, a white blood count of – 15,900 cells per cu mm with 57 % neutrophils, 42% lymphocytes, and 1% eosinophils. C-reactive protein was 23 mg/L. Cerebrospinal fluid (CSF) analysis showed glucose of 10 mg/dL, protein – 294 mg/dL, and lymphocyte cells – 3 which were suggestive of pyomeningitis. Neonate was initiated on meningitis dose of Inj. meropenem (40 mg/kg/dose every 8 hourly IV) and Inj. amikacin (15 mg/kg/dose every 24 hourly IV) and oral paracetamol 15 mg/kg/dose. Neonate was continued on expressed breast milk through an orogastric tube. There was no further fever episode. First blood and CSF culture on blood agar grew *E. meningoseptica*, which was sensitive to piperacillin-tazobactam, ciprofloxacin, levofloxacin, cefepime, gentamicin, amikacin, cotrimoxazole, and cefoperazone sulbactam and was resistant to meropenem.

As per the sensitivity pattern, Inj. meropenem was stopped and Inj. levofloxacin (10 mg/kg per dose every 12 hourly) was started, and amikacin was continued. From the day of life (DOL) 16 onward, the neonate was noted to have refractory multifocal clonic seizures involving all 4 limbs lasting for 1–2 min each. Initially was loaded with Inj. levetiracetam (50 mg/kg IV) followed by Inj. phenytoin (20 mg/kg, IV), Inj. sodium valproate (20 mg/kg IV), and Inj. midazolam (0.2 mg/kg/hr IV). On seizure control, the neonate was continued on the above drugs in maintenance dose.

Repeat blood culture after 7 days of levofloxacin and amikacin showed no growth but repeat CSF culture showed the same organism with a different antibiotic sensitivity. The organism was sensitive to ceftriaxone, cefepime, gentamycin, amikacin, cotrimoxazole, and cefoperazone sulbactam and resistant to – meropenem, piperacillin-tazobactam, ciprofloxacin levofloxacin, and imipenem. Inj. Levofloxacin was stopped and Inj. Cefepime (50 mg/kg/dose IV every 12 h) was added.

The culture swabs of the feeding bottle and breast pump used at home grew multiple organisms including Acinetobacter, Pseudomonas, and Klebsiella. The culture of tap water used for disinfection had no growth. Serial neurosonogram was suggestive of non-obstructive hydrocephalus. There was progressively increasing head circumference (HC) every 4 days since admission from 31.5 cm→ 32.5 cm→ 34 cm→ 35 cm with progressively worsening Levene index which was >4 mm above the 97 centile (2.0 cm→2.1 cm→2.4 cm→2.8 cm). A computed tomography scan showed gross non-communicating hydrocephalus [Figure 1] with an Evans index of 0.63 with thinned-out brain parenchyma [Figure 2].

Due to serially increasing HC and worsening neurological status and neurosonogram showing increasing Levene index above the 97th centile, a therapeutic ventricular tap was done thrice and 15 mL/kg of CSF was drained. In view of worsening sensorium and poor spontaneous respiratory efforts, the neonate was mechanically ventilated from

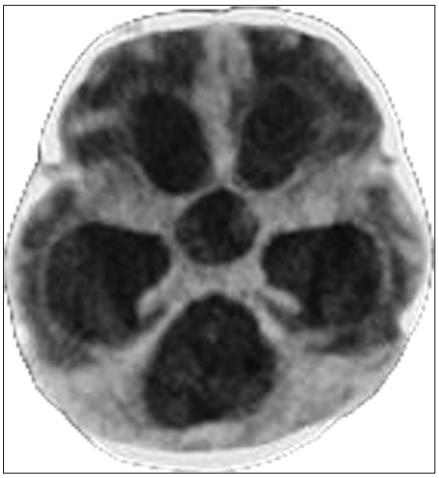

Figure 1: Computed tomography brain showing grossly dilated ventricles.

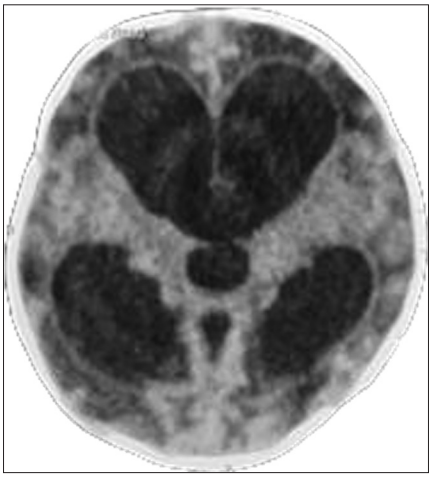

Figure 2: Computed tomography brain showing gross enlargement of all ventricles suggestive of non-obstructive hydrocephalus with thinned out brain parenchyma.

Table 1: CSF culture and blood culture report.

DOL	CSF routine (cells)	CSF protein (mg/dL)	CSF sugar (mg/dL)	CSF culture	Blood culture
DOL-14	3 Lymphocytes	294	10	*Elizabethkingia meningoseptica*	*Elizabethkingia meningoseptica*
DOL-21	0	294	23	*Elizabethkingia meningoseptica*	*Elizabethkingia meningoseptica*
DOL-23	0	294	30	*Elizabethkingia meningoseptica*	
DOL-30	0	294	28	*Elizabethkingia meningoseptica*	

CSF: Cerebrospinal fluid, DOL: Day of life

DOL 23. The neonate continued to be evaluated by a multidisciplinary team of neurosurgeons, occupational therapists, and physiotherapists. Since there was no improvement noted, a plan for insertion of the Ommaya reservoir and use of intraventricular antibiotics was made.

Repeat CSF after 7 days of sensitive antibiotics, again grew the same organism with a different antibiotic sensitivity pattern. The organism was sensitive to – cotrimoxazole, cefoperazone sulbactam, and minocycline and resistant to cefepime, amikacin, meropenem, piperacillin-tazobactam, ciprofloxacin, levofloxacin, imipenem, gentamicin, and ceftazidime. Inj. cefepime and Inj. amikacin were stopped, and the neonate was started on Inj. cefoperazone sulbactam (100 mg/kg/day in two divided doses) with an oral cotrimoxazole (5 mg trimethoprim/kg/dose 12 hourly PO).

There was progressive deterioration of neonate's neurological status and developed refractory septic shock. Before the insertion of Ommaya reservoir, the neonate had worsening septicemia, refractory shock, and succumbed to sepsis on day 39 of life.

DISCUSSION

E. meningoseptica is a ubiquitous Gram-negative non-motile, non-fermenting oxidase-positive bacillus.[1] This organism is commonly found in soil and water and has the ability to survive even in chlorinated water.[2] It is not a part of human microbiological flora and a rare cause of pyomeningitis.[3]

This organism is often reported as a hospital-acquired infection in premature neonates and in those with prolonged hospital stay, prior exposure to multiple antibiotics, and presence of invasive devices such as an indwelling central venous catheter.[4,5] There are case reports of outbreaks due to contamination of intravenous fluids, antibiotic solutions, infant formula, and water supply.[6] Despite the organism being ubiquitous in the environment, the cases of community-acquired meningitis reported in neonates are less. The source of infection in our case probably was the feeding bottle and breast pump due to improper disinfection technique.

The rarity of the organism and its multidrug resistance and antimicrobial susceptibility makes standard treatment recommendations difficult. Neonatal meningitis caused by it has a high mortality rate of up to 57 %.[7] Hydrocephalus is reported in 69% of survivors.[8] The major post-infectious sequelae such as deafness and developmental delay have led to the use of multiple antibiotics in the management of these cases, and also, there is a lack of protocolized effective treatment regimens.

There are a number of concerns while treating this organism: Frequent escalation of antibiotics, unreliable *in vitro* sensitivity, delay in response, longer course of treatment, persistence of CSF and neurosonogram abnormalities, and doubtful CSF penetration of sensitive antibiotics.[9] *E. meningoseptica* demonstrates *in vitro* resistance to many antibiotics but changing pattern of resistance as seen in our case is not reported till date.

The reason for this resistance is attributable to two β-lactamases that are produced, namely, extended-spectrum β-lactamase and a carbapenem hydrolyzing metallo-β-lactamase. In our index neonate, the organism was resistant to meropenem the first- line anti-meningitis drug of our unit in both blood and CSF cultures.[10] Despite being a Gram-negative bacillus, it is extremely sensitive to antibiotics used to treat Gram-positive infections, including vancomycin, rifampicin, piperacillin-tazobactam, newer fluoroquinolones, minocycline, and tigecycline.[11]

Recent studies have shown fluoroquinolone to be beneficial, which can be attributed to its improved pharmacokinetics. Compared to ciprofloxacin, the antibiotics sparfloxacin, clinafloxacin, and levofloxacin have greater action.[12] However, the organism in our case was resistant to piperacillin-tazobactam initially followed by the development of resistance to fluoroquinolones, amikacin, and cefepime in the later part of the hospital stay. Recently, there has been an emerging role in the combination of systemic antibiotics with intraventricular vancomycin.[9]

The extremely high virulence, its ubiquity, lack of protocolized treatment regimens, and the difficulty in predicting the clinical outcome based on *in vitro* sensitivity have made the treatment extremely challenging. To this list of difficulties, a changing antibiotic sensitivity pattern and

diagnosis of community-acquired meningitis is surely a new challenge and a concern of public health importance.

CONCLUSION

Meningitis and life-threatening septicemia caused by *E. meningoseptica* are rare but have been reported previously in preterm neonates and NICU outbreaks. This case adds a new dimension of a community-acquired etiology and, thus, illustrates the importance of increasing the awareness of the widespread presence of this organism in the environment and an urgent need for re-emphasizing the promotion of safe, careful cleaning, and disinfection of breast pump equipment at home. Resistance to commonly used NICU anti-meningitis antibiotics and the changing antimicrobial resistance make this organism even more virulent. *E. meningoseptica* is an emerging potential source of neonatal infection which needs to be further studied in large case series from low- and middle-income countries and this might aid in preventing fatality and potentially devastating complications as in our index neonate.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The author(s) confirms that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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