

***Elizabethkingia meningoseptica* infection in neonates: Two case reports from the Eastern region of Oman**

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Abstract

Elizabethkingia meningoseptica is a gram-negative rod-shaped bacterium commonly found in soil and water. This organism is associated with nosocomial infections, especially in neonatal wards, as it has been isolated from contaminated medical equipment's. prompt diagnosis and early institution of appropriate combination therapy for prolonged period are crucial in management of such infections. Herein, we describe two premature neonates admitted to our special care baby unit at 31, and 36 weeks old, respectively, who were diagnosed with neonatal bacterial sepsis. In both patients, blood and/or cerebrospinal fluid cultures indicated that *E. meningoseptica* was the causative organism. This bacterium is generally resistant to multiple antibiotics, including combination therapy. Therefore, *E. meningoseptica* can cause severe infection with a high risk of mortality and neurological sequelae in neonates. Intensive care and multidisciplinary interventions and involvement of infection control team are crucial for effectively managing and preventing these infections.

Keywords: *Elizabethkingia meningoseptica*, prematurity, neonatal sepsis.

Introduction:

Premature neonates are at risk for *Elizabethkingia meningoseptica* infections, which include meningitis and sepsis.^(1,2) Normally found in soil and water, *E. meningoseptica* has also been isolated from hospital surfaces and medical devices, such as ventilators; thus *E. meningoseptica* has increasingly been recognized as the causative organism of nosocomial infections.⁽³⁾ *E. meningoseptica* is a gram-negative, non-fermentative, oxidase-positive, non-motile, aerobic bacillus that tests positive for catalase and urease.^(4,5) The risk factors for *E. meningoseptica* infection include indwelling central venous catheters, prematurity, immunosuppression, prolonged and prior exposure to higher antibiotic concentrations.⁽⁶⁾ *E. meningoseptica* resist β -lactamases antibiotics by two different ways (intrinsic class A extended-spectrum serine- β -lactamases and inherent class B metallo- β -lactamases), which render it resistant to a broad range of antimicrobials that are routinely used for empiric therapy of infections caused by Gram-negative organisms⁽⁷⁾ Therefore, the selection of appropriate antibiotic treatment is clinically difficult. Herein, we describe our experience with two cases of neonatal *E. meningoseptica* infection.

Case I:

A female infant born as one of two twins at 31 weeks' gestation with a birthweight of 1.5 kg. No resuscitation was required. She developed respiratory distress and was connected to continuous positive airway pressure. Her chest X-ray showed signs of respiratory distress syndrome, so she was intubated and surfactants were administered. Few hours later the baby improved and extubated and shifted to nasal cannula oxygen. No central lines were required. Feeds were started and tolerated. At day six of life, the baby was less active and lethargic. Based on septic work up (complete blood cell count

Initial blood tests showed (white cell count $18.5 \times 10^3/\text{uL}$) (reference range (RR) 6–20 $\times 10^3/\text{L}$) with neutrophils ($12.4 \times 10^3/\text{uL}$ neutrophils) (RR 1 – $8.5 \times 10^3/\text{uL}$), haemoglobin of 11.8 g/dL (reference range 10.0–14.1 g/dL,) and (platelet count $411 \times 10^3/\text{uL}$ (RR, 150 – $450 \times 10^3/\text{uL}$)). C reactive protein was 15.7 mg/dL (RR 0 – 5mg/L), and blood cultures were collected and started empirically on ampicillin and gentamycin. Lumbar puncture was also performed. She showed initial improvement in terms of improved activity, no fever, and feeding was tolerated, but later her condition deteriorated as she developed convulsions and apnoea which required intubation. Her blood culture initially reported a non-fermentative gram negative bacteria sensitive to tazocin. The test used is disc diffusion method according to CLSI (clinical and laboratory standard institute), so tazocin was started. Blood culture was sent to referral laboratory to identify the organism and *E. meningoseptica* was detected by Vitek II (BioMerieux, France). Cerebrospinal fluid A lumbar puncture (LP) was performed and CSF analysis revealed hypoglycorrhachia (glucose 1.1 mmol/L (2.8 – 4.4mmol/L), WBC $2000/\text{mm}^3$ (NR 0–5) and elevated proteins (280 mg/dL (RR 15 – 45 mg/dl). Blood culture indicated the same organism sensitive to levofloxacin and rifampicin so these antibiotics were initiated and the ID team was involved. Head ultrasound (US) was normal. The infant's general condition improved, and she was extubated at day 15 of life. Lumbar puncture was repeated after three weeks of antibiotics and showed no organisms but protein was high in the CSF (27.2) mg/dl with low sugar (1.57) mg/dl so antibiotics (levofloxacin and rifampicin) were continued for another two weeks, at which point LP was repeated and showed improvements. The baby received a total of seven weeks of antibiotics and was discharged in stable condition. At follow-up, she had normal growth and development for her age.

Case II:

Case II is a male infant born at 36 weeks' gestation with a birthweight of 2.5 kg. At day eight of life, the baby came from home with poor feeding, fever, and vomiting. Physical examination was unremarkable, and septic work up was done (CBC, CRP, and blood and urine cultures; but LP was not done because the parents refused). (complete blood cell count Initial blood tests showed (white cell count $16.7 \times 10^3/\text{uL}$) (reference range (RR) $6-20 \times 10^3/\text{L}$) with neutrophils ($7.4 \times 10^3/\text{uL}$ neutrophils) (RR $1 - 8.6 \times 10^3/\text{uL}$), haemoglobin of 11.73 g/dL (reference range 10.0–14.1 g/dL,) and (platelet count $363 \times 10^3/\text{uL}$ (RR, $150 - 450 \times 10^3/\text{uL}$)). C reactive protein was 44.8 mg/dL (RR 0 – 5mg/L), He was started empirically on ampicillin and gentamicin. Head US was normal. Urine culture showed *Klebsiella pneumonia*, so antibiotics were changed to cefotaxime. His blood culture showed *E. meningoseptica* sensitive to ciprofloxacin and minocycline so ciprofloxacin was added. The case was discussed with the infectious disease team who suggested a brain CT scan and the addition of vancomycin to the antibiotic course. The infant continued to be hemodynamically stable and tolerated feeding. Head CT was normal, and a peripherally inserted central catheter line was inserted for continued antibiotic administration. The infant completed 21 days of antibiotics. After the antibiotic course, blood culture was negative and the infant was discharged. His condition has remained well with no neurological sequelae.

Discussion:

Neonatal bacterial meningitis (NBM) is an uncommon but serious infection with high mortality and the morbidity remains high among survivors. ⁽⁸⁾ The types and distribution of causative pathogens differ according to birth, gestational age, postnatal age, and geographic region with Group B *Streptococcus* being the most common cause of neonatal sepsis and meningitis since the early 1980s. ⁽⁹⁾ Premature labour is a risk factor for meningitis because most maternal immunoglobulins cross the placenta after 32

week's gestation, so infants born extremely preterm are at significantly higher risk for infections.⁽¹⁰⁾ In Oman, prematurity account for 63% of death in which sepsis due to gram negative bacteria was a major cause. ⁽¹¹⁾ *E. meningoseptica* is an emerging pathogen for nosocomial infections including sepsis and meningitis. It is rare but is associated with high mortality because of its antibiotic resistance and difficult diagnosis.⁽¹²⁾ As a primarily opportunistic pathogen, *E. meningoseptica* mainly infects newborns and immunocompromised hosts from all age groups. Environmental studies have revealed that the organism can survive in chlorine-treated municipal water supplies, often colonises sink basins and taps, and has become a potential reservoir for infections in hospital settings.⁽¹³⁾ As in our cases, premature newborns weighing <2,500 g are at higher risk of *E. meningoseptica* infection.

The source of an *E. meningoseptica* outbreak can be detected by obtaining cultures from food and infant formulas, wet areas, dry surfaces, equipment, and the hands of healthcare workers in contact with infected patients. We isolated the organism from a water tank in our institution, which emphasizes the importance of obtaining cultures on a periodic basis is necessary.⁽¹⁴⁾ Changing the prescribing policy for empiric antibiotics and protocols for admissions to the neonatal unit, in addition to thorough disinfection of the unit have been recommended as measures to eradicate *E. meningoseptica* outbreaks in pediatric wards.⁽²⁾ Infection control with milder measures has been described in other studies, including alcoholic hand rubs after washing hands, toileting of babies with sterile water instead of tap water; and repairing, cleaning, super chlorinating, and isolating water tanks from all hospital feeder tanks and changing the sink taps. Continuous training should be implemented to reemphasize hand washing and contact precautions to all hospital staff. ^(15,16)

The bacterial isolates in our cases were sensitive to ciprofloxacin, (piperacillin/tazobactam) and vancomycin. Recent studies have demonstrated the effectiveness of fluoroquinolones, due to its superior pharmacokinetics compared to hydrophilic antimicrobials, such as beta-lactams. ⁽¹⁷⁾ Sparfloxacin, clinafloxacin, and levofloxacin have shown better activity against *E. meningoseptica* than ciprofloxacin. Rifampin has been used as part of combination therapy for the treatment of persistent infection. Vancomycin alone or in combination with other agents like rifampin, has been successful for the treatment of meningitis in infants. ⁽¹⁸⁾ additional studies are required to verify this. Finally, our infection control measures in the special care baby unit were successful as no further *E. meningoseptica* infections were reported for the last two year ago.

Conclusion:

Nosocomial infections caused by *E. meningoseptica* is an increasing problem in healthcare settings especially for immunocompromised patients. Mainly because of the ability to survive in environment and the antimicrobial resistance nature. It is crucial to increase the capacity of laboratories for the diagnosis of these bacterium and to implement a multidisciplinary approach for the care of infected neonates. our experience has demonstrated the need for combined antibiotic strategies for better outcomes.

Availability of data

Data are available on request.

Conflict of interest

None

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Authors' contribution

All authors contribute equally.

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