

Elizabethkingia meningoseptica infection in neonates: a threat and clinical challenge

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ABSTRACT:

- **Objective:** Elizabethkingia meningoseptica is a multidrug resistant gram-negative bacillus that is commonly associated with nosocomial infection in neonates. Prematurity and compromised immune system are a known risk factor for E. meningoseptica infection. It has been isolated in the hospital environment, water supplies, disinfectants and medical devices. We report 3 cases of neonatal infection by E. meningoseptica over a period of three years (2018-2020) in our Neonatal Intensive Care Unit (NICU). We encountered one case each of pneumonia, meningitis and septicemia. Infection associated with E. meningoseptica can be life-threatening if appropriate antibiotics are not prescribed. As this organism is multi drug-resistant, failure to identify this pathogen may lead to therapeutic failure. E. meningoseptica is intrinsically resistant to wide range of antibiotics used to treat other common pathogenic gram-negative bacteria; however, they are sensitive to fluoroquinolones and glycopeptides that are used for gram positives. In view of its multidrug resistant nature and ability to easily infect preterm and very low birth weight neonates, prompt diagnosis should be made and appropriate reinforcement of infection control measures should be considered to reduce morbidity and mortality.
- **Keywords:** Elizabethkingia meningoseptica, Neonatal sepsis, Rifampicin, Chrysobacterium sps.

INTRODUCTION

Elizabethkingia meningoseptica belonging to the family Chrysobacterium is a gram-negative, aerobic, glucose non-fermenting, non-motile, oxidase and catalase positive bacilli^{1,2}. Six serotypes (A-F) of E. meningoseptica have been isolated since its first identification in 1959, of which type C being responsible for most cases of infection. E. meningoseptica—the most pathogenic member of the family can cause neonatal meningitis, bacteremia and pneumonia especially in preterm neonates. It has been isolated from hospital water supplies, sinks, taps, disinfectants, medical devices including feeding tubes, catheters, respirators, intubation tubes, humidifiers and incubators used for newborns. Infections usually occur

as outbreaks if no containment measures are taken^{3,4}. E. meningoseptica infection presents mostly as meningitis, bacteremia, skin and soft tissue infection, pneumonia, catheter associated infections and urinary tract infections in neonates, infants and immunocompromised patients^{3,5}. Chrysobacterium sps are associated with high morbidity and mortality (47-52%) and this risk grows high as they are known to exhibit resistance to beta-lactams, carbapenem, aztreonam, aminoglycosides, trimethoprim sulfamethoxazole and tetracyclines^{1,6}. Most Chrysobacterium are resistant to beta lactams and carbapenems as they possess two types of β lactamases namely class A Extended Spectrum Beta Lactamase (ESBL) and Class B Metallo Beta Lactamase (MBL). Harboring and producing two types of MBL (blaB and



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GOB genes) and chromosomally makes it intrinsically resistant to most beta lactams and carbapenem class of antibiotics¹. These organisms being resistant to all conventional antibiotics used to treat neonatal meningitis as ampicillin, meropenem and gentamicin make it a difficult bug to eradicate³. *E. meningoseptica* exhibits good susceptibility to many antibiotics used for gram positive cocci especially vancomycin and/or rifampicin containing regimen with or without fluoroquinolones¹.

CASE REPORT

Case 1

A premature female infant born at 31+3 weeks gestational age with a birth weight of 1.76 Kg was treated in an outside hospital, transferred to our NICU at 31 days of life with persistent desaturation and prolonged ventilator support. Clinical examination revealed a dull and lethargic baby with high ventilatory requirement. Initial counts were normal and the neonate exhibited features of bronchopneumoniae in X-ray. Using sterile aseptic technique blood culture was obtained and the neonate was started on meropenem and vancomycin empirically, as this neonate had exposure to multiple first line antibiotics. Inotropic support (dopamine and dobutamine) was required to managed sepsis associated shock. Echocardiogram showed moderate Pulmonary Artery Hypertension and moderate tricuspid regurgitation for which the baby was put on high frequency oscillatory ventilation along with inhaled nitric oxide. Considering prolonged ventilation respiratory viral panel was sent and was positive for Respiratory syncytial virus.

In spite of continuing antibiotics baby had elevated counts (WBC: 34400 cells/mm³), Thrombocytopenia (Platelet: 12000 cells). Hence repeat blood culture was done and it was positive for *Candida albicans* for which injection fluconazole was administered. Culture from Bronchio Alveolar Lavage (BAL) grew gram negative bacilli that were isolated as *E. meningoseptica* at 48 hours and was resistant to piperacillin tazobactam, carbapenems, aminoglycosides, colistin, co-trimoxazole but sensitive to cefoperazone sulbactam (MIC 16 mcg/ml), levofloxacin (MIC 0.5 mcg/ml), ciprofloxacin (MIC 1 mcg/ml) and minocycline (MIC <1 mcg/ml). The baby was started on intravenous ciprofloxacin. The baby condition gradually deteriorated with worsening clinical and neurological status. In spite of all measures taken neonate did not survive the resuscitation and succumbed at day 45 of life.

Case 2

A Preterm 35+2-week male neonate weighing 2.05 Kg was delivered through lower segment caesarean section due to premature rupture of membrane was initially treated in an outside hospital for routine preterm care. Baby was referred to our NICU with a history of desaturation, hyperglycemia (RBS:167 mg/dl), tachycardia (208 beats/

min), lethargy and poor feeding. In view of late onset sepsis and meningitis, blood and CSF samples were collected and sent for laboratory and microbiological examination. On examination baby had tachycardia (HR: 190 beats / min), respiratory rate 54 breaths/min, and encephalopathy. Considering late onset sepsis after obtaining blood culture aseptically, antibiotics were escalated to Meropenem. Sepsis screening revealed total count 15500 cells/cumm, Platelet – 236000 cells, CRP 2 mg/dl (negative). Lumbar puncture was done considering meningitis and CSF samples were sent for microbiological analysis including cell count, protein, sugar, gram stain and culture. CSF was cloudy with CSF protein 87.4 mg/dl, glucose 57 mg/dl, RBC 130 cells/mm³, WBC 30 (Polymorphs 05% and Lymphocytes 95%) and CSF culture was positive for *E. meningoseptica* at 72 hours confirming the clinical diagnosis of bacterial meningitis. Isolated organism was sensitive to levofloxacin (MIC 2 mcg/ml), minocycline (MIC 2 mcg/ml), vancomycin (MIC 2 mcg/ml), rifampicin (MIC 1 mcg/ml) and cotrimoxazole (MIC 40 mcg/ml) and moderately sensitive to cefoperazone sulbactam (MIC 32 mcg/ml) and resistant to Beta-lactams with Beta lactamase Inhibitors (BL-BLIs), cephalosporins, aminoglycosides and ciprofloxacin. Antibiotics were changed to intravenous levofloxacin and vancomycin along with oral rifampicin. After starting specific therapy baby activity improved and repeat CSF analysis had protein 87.3 mg/dl, glucose 44 mg/dl with WBC 10 cells/cumm (all are lymphocytes). Antibiotics were administered for 4 weeks. Baby improved well clinically and at 5 months follow up, he was noted to have good weight gain and neurodevelopmental outcome.

Case 3

A 10 days old preterm (32+2 weeks) male neonate weighing 1.4 kg admitted for routine preterm care. Considering risk of early onset sepsis, neonate was started on first line antibiotics (ampicillin and amikacin). Since the cultures came out sterile, antibiotics were stopped and baby was put on full direct breastfeeding. On day 7 of life baby was found to have severe hypothermia, seizure, lethargy, hypoglycemic and bulging fontanelle. Baby was shifted to our unit for further care. Intravenous fluids and meropenem 20 mg/kg/dose Q8h were started. Blood counts revealed TC 18200 cells/cumm, Thrombocytopenia (Platelet 40000 cells), CRP: 16 mg/dl (Positive) and CSF examination revealed WBC: 250 cells of which 65% were polymorphs. CSF sugar was < 10 mg/dl and protein 524 mg/dl. Blood culture had GNB growth at initial incubation and the organism was isolated to be *E. meningoseptica* after 48 hours and sensitive to ciprofloxacin (MIC 1 mcg/ml), levofloxacin (MIC 1 mcg/ml), minocycline (MIC ≤ 1 mcg/ml), vancomycin (MIC 2 mcg/ml) & rifampicin (MIC 1 mcg/ml), moderately sensitive to cefoperazone sulbactam (MIC 32 mcg/ml) and resistant to BL-BLIs, cephalosporins, aminoglycosides and cotrimoxazole. The baby was started on injection ciprofloxacin, vancomycin and oral rifampicin for 4 weeks. During

therapy baby improved clinically and symptomatically. Feeding establishment was done, repeat counts and CSF analysis done after 7 days of therapy was within normal limits. Serial head circumference monitoring and neurosonogram were normal. At 5 months follow up baby was developmentally well with adequate weight gain.

DISCUSSION

Prematurity is a primary risk factor for *E. meningoseptica* infection. *Chrysobacterium sps* are rare emerging pathogen responsible for health care associated infection mainly seen in patients with prolonged hospital stay or indwelling devices (endotracheal tubes). Bacteremia and pneumonia are more common manifestations but also been implicated in meningitis, endocarditis, skin and soft tissue infections, abdominal infection and eye infection in immunocompromised hosts. Treatment should be based on MIC results from microbiological analysis. Compared with other pathogenic organisms, *E. meningoseptica* occurs as a late onset infection. In our study, the time interval between the admission of neonates to hospital and infection with *E. meningoseptica* was an average of 16 days (with a range of 7 to 31 days).

Out of 3 neonates, 2 recovered with antibiotic therapy. One neonate succumbed during therapy and the cause may be due to concurrent *Candida* sepsis with *E. meningoseptica* pneumonia. Patients with *E. meningoseptica* infection have poor prognosis and delay in the use of appropriate antibiotics may further worsen the situation. All the neonates were treated with vancomycin, fluoroquinolone with rifampicin. In our series levofloxacin and minocycline were the most sensitive antibiotics. Shailaja et al⁸ reported 9 neonates with meningitis by *E. meningoseptica*. Clinically the isolates were analyzed using 16S ribosomal RNA technique and were resistant to betalactams, cephalosporins, aminoglycosides, trimethoprim, carbapenem but were sensitive to vancomycin and one was sensitive to ciprofloxacin. 6 of 9 neonates died despite treatment with vancomycin⁷. In our analysis, the infection was presumed to be nosocomial in origin. *E. meningoseptica* is widely distributed in nature and it is very challenging for both clinicians and microbiologists to identify the etiology and source of infection. It is resistant to commonly used antibiotics commonly used to treat gram negative bacteria and only limited number of antibiotics are available for treatment. Infection of this pathogen is potentially fatal unless diagnosed and treated early. Awareness among clinicians about the organism along with correct identification of species and sensitivity is required to reduce morbidity and mortality associated with *E. meningoseptica*.

CONCLUSIONS

E. meningoseptica increasingly being recognized as a pathogen in hospital environment. Multidrug resistant phenotype of this bacteria warrants the use of early, appropriate, sensitive antibiotics. Preterm neonates,

immunocompromised patients and patients who are exposed to long term antibiotics are at high risk with grave consequences once infected with *E. meningoseptica*. Equipment used in intensive care units has become potential reservoir for infections in hospital environment. *E. meningoseptica* has unusual resistance pattern as they are resistant to many antimicrobial agents commonly used to treat infection by gram negative bacteria (aminoglycosides, carbapenem, chloramphenicol) but are susceptible to agents used to treat infections by gram positive bacteria (rifampicin, fluoroquinolones and glycopeptides). This gram-negative pathogen is vancomycin and rifampicin sensitive but resistant to colistin. Early identification and strict isolation precautions are mandated in reducing the outbreak of this opportunistic pathogen. Inservice training for handwashing and proper infection control interventions should be educated to all health care workers to control outbreaks of this opportunist.

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CONTRIBUTOR'S STATEMENT:

Gayathiri Govindaraju collected data and drafted the initial manuscript, Dr Balakrishnan Rajaiah is accountable for all aspects in this work, ensured appropriate data collection and resolved query related to this work, Dr Srinivas Ramakrishnan coordinated, supervised and critically revised the manuscript.

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CONFLICTS OF INTEREST:

The authors declare that they have no conflict of interests.

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