A rare case of *Elizabethkingia meningoseptica* infection in a neonate

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**ABSTRACT**

**Background:** Elizabethkingia infections were reportedly rare, but if it was found, it had been known to cause neonatal meningitis, bloodstream infections and respiratory infections. *Elizabethkingia meningoseptica* had a unique antibiotic susceptibility pattern, usually resistant to most antibiotics. Elizabethkingia infections were associated with a high mortality rate because of the lack of effective therapeutic regimens, antibiotic resistance and virulence.

**Case Presentation:** Fourteen days old boy patient came with the chief complaint of seizure, which occurred twice. Before the seizure, the patient had a fever with the highest temperature was 39°C. The patient looked lethargic, tended to sleep more often, cried occasionally and was not as active as previously. Septic marker revealed an Immature to Total neutrophil (IT) ratio of 0.2 and C-Reactive Protein (CRP) 49.30 mg/dL. A blood smear examination showed toxic granules, vacuolization of the leucocyte and reactive thrombocytosis. Cerebrospinal fluid analysis revealed a cell number of 2520 cell/μL, polymorphonuclear (PMN) cell 80%, mononuclear (MN) cell 20%, Nonne and Pandy was positive, protein level at 300 mg/dL and cerebrospinal fluid glucose level below 20 mg/dL. The patient was initially diagnosed with sepsis and meningitis and was given ampicillin and gentamicin.

**Conclusion:** *Elizabethkingia meningoseptica* was a rare case, and the nature of this bacteria was resistant to multiple antibiotics. Treatment should be considered carefully.

**Keywords:** Neonates, sepsis, meningitis, *Elizabethkingia meningoseptica*.


**INTRODUCTION**

Elizabethkingia is a bacterial genus commonly detected in the environment but rarely causes human infection. However, following an increased incidence of Elizabethkingia infections among patients in intensive care units since 2004, Elizabethkingia has been identified as an emerging pathogen in hospital settings. Elizabethkingia was first discovered in 1959 by Elizabeth O. King. King was an American bacteriologist working on an uncultivated bacteria associated with infant meningitis. The genus Elizabethkingia has six species which are *Elizabethkingia anophelis*, *Elizabethkingia meningoseptica*, *Elizabethkingia bruuniana*, *Elizabethkingia miricola*, *Elizabethkingia occulta* and *Elizabethkingia ursingii*. Based on genome sequence analysis, a recent report indicates the greater ability of *Elizabethkingia meningoseptica* to form biofilm compared than other species. It consists of yellow pigment—producing, non-motile, catalase—positive, oxidase—positive, non—glucose—fermenting, and gram—negative bacilli. ¹–³

Elizabethkingia infections have been known to cause neonatal meningitis, bloodstream infections and respiratory infections. Worldwide infections caused by *Elizabethkingia meningoseptica* were reportedly rare, but if it was found, mostly among neonates as well as hospitalized patients with existing underlying infections. Research showed 283 cases of *Elizabethkingia meningoseptica* reported from 28 countries between 1944 to 2017. About 76% were neonates aged 0–1 month and 74% were diagnosed with meningitis.¹–³ *Elizabethkingia meningoseptica* has a unique antibiotic susceptibility pattern, usually resistant to most of the antibiotics used against gram-negative bacteria but often susceptible to agents generally used to treat infections caused by gram-positive bacteria. This often leads to inappropriate choice of antibiotics for initial empirical
therapy and results in treatment failures. Elizabethkingia infections are associated with a high mortality rate because of the lack of effective therapeutic regimens, antibiotic resistance and virulence. The mortality rate is approximately 30%.

We present a case of an infant with late-onset neonatal sepsis and neonatal meningitis due to *Elizabethkingia meningoseptica*.

**CASE REPORT**

A 14 days boy patient was referred from “A” hospital with the diagnosis of meningitis and chief complaint of seizure. The mother said the patient had a seizure in “A” hospital 2 days before being referred to “B” hospital. The seizure with both hands, feet, and body stiffened, eyes rolled upward, and lasted for around 10-15 seconds, with a temperature of 38.9°C. The seizure ended spontaneously without any medication, and after the seizure episode, the patient cried immediately. The patient had a fever since 6 days before admission at “A” hospital (age 8 days old) with the highest temperature was 39°C and improved with antipyretic drugs with the lowest temperature was 37.1°C. The fever fluctuated and occurred all day.

When the patient arrived at “B” Hospital, the patient looked lethargic, tended to sleep more often, cried occasionally and was not as active as previously. He also had a fever of about 38.2°C. One hour after admission, he had a seizure with the same characteristic for less than 1 minute. The seizure ended spontaneously, and after the seizure episode, he was alert. There was no profuse vomiting, shortness of breath, bluish appearance, yellowish skin and abdominal distention. His feeding activity decreased, with sucking weakening since 6 days before admission. The patient’s mother said he had no defecation or urination changes.

The patient was the last child of three siblings. His first older sister was 8 years old, and the second sister was 3 years old. His siblings were healthy. His parents did not have a severe illness history of hypertension, diabetes mellitus and another chronic disease. This was the mother’s third pregnancy at 28 years old. She routinely checked her pregnancy. Ultrasonography examination revealed the normal condition of the baby. In the first trimester, the mother had a vaginal discharge of white color and foul smell. The mother did not treat that complaint until the baby was born. The mother had never smoked or consumed alcohol, herbal drugs, or other drugs. She only took multivitamins given by primary health care and obstetrician routinely. The history of toxoplasma, rubella, cytomegalovirus and herpes (TORCH) infections was unknown.

The patient was delivered by cesarean section with an indicated breech position. The baby was born at 36-37 weeks of gestational age with a birth weight of 2640 grams (25th until 50th percentile of the Lubchenco curve), a length 50 cm (75th until 90th percentile of the Lubchenco curve) and a head circumference 31 cm (10th until 25th percentile of the Lubchenco curve). There were 2 minor risk factors for infection (gestational week <37 weeks and history of vaginal discharge). The patient was said to cry immediately after birth. There was no history of delivery complications. On physical examination, there were no congenital abnormalities.

Laboratory findings at “A” hospital revealed white blood cells (WBC) 10.62x10^9/μL (neutrophils 79%, lymphocytes 8.9%), hemoglobin (HB) 14.3 g/dL, hematocrit (HCT) 43.10%, platelets (PLT) 279x10^9/μL, Immature to Total neutrophil (IT) ratio 13. Cerebrospinal fluid analysis revealed cell number of 2520 cell/μL, polymorphonuclear (PMN) cell 80%, mononuclear (MN) cell 20%, with Nonne and Pandy were positive, protein level at 300 mg/dL, and cerebrospinal fluid glucose level below 20 mg/dL. The patient was initially diagnosed with sepsis and meningitis and was given ampicillin 125 mg every 12 hours (47 mg/kg/times) and gentamicin 12 mg every 24 hours intravenously. Blood and cerebrospinal fluid culture came out on day 4th of antibiotics, isolated *Elizabethkingia meningoseptica* and significant as the infection-causing agent. The antibiotic sensitivity of the blood culture was ciprofloxacin and levofloxacin. The antibiotic sensitivity of the cerebrospinal fluid culture was levofloxacin.

At admission to “B” hospital (14 days old), the patient's weight was 2780 grams (10th-50th percentile), the length was 52.2 cm (50th-90th percentile) and the head circumference was 33 cm (10th-50th percentile) of the Fenton growth chart. Physical examination revealed weak activity; the temperature ranged between 37-39°C, pulse rate 150-155 beats/minute, respiratory rate 40-45 breaths/minute, and oxygen saturation range 95-97% in room air. The patient’s head revealed a major fontanelle opened bulging. Lung and cardiac auscultation revealed no rales, wheezing, or heart murmur. There was no abdominal distention and no neurological deficit.

Laboratory findings at B hospital revealed WBC 13.42x10^9/μL (neutrophils 7.58 (56.50%), lymphocytes 2.75 (20.5%), HB 9.9 g/dL, HCT 29.40%, PLT 57x10^9/μL, IT ratio 0.2 and C-Reactive Protein (CRP) 49.30 mg/dL. A blood smear examination showed toxic granules, vacuolization of the leucocyte and reactive thrombocytes. The patient was assessed with late-onset neonatal sepsis and neonatal meningitis due to *Elizabethkingia meningoseptica*.

Cerebrospinal fluid analysis and laboratory tests were evaluated according to clinical evaluation (Table 1 and Table 2).

The patient was treated at the level II neonatal ward. Fluid requirements were 120 ml/kg/day fulfilled by enteral nutrition with on-demand breastfeeding, at least 42 ml every 3 hours. The patient was continued to be given a severe dose of ampicillin 300 mg/kg/day every 6 hours intravenously and gentamycin 5 mg/kg/times every 24 hours intravenously for 12 days because, on the second evaluation, the cell of the cerebrospinal fluid was improved. On the third evaluation of the septic marker, the thrombocyte was increased. On the third evaluation of cerebrospinal fluid analysis, there was an increasing protein and no significant improvement in the cell and glucose. With that consideration, the antibiotic was changed to levofloxacin 10 mg/kg/times every 12 hours intravenously for 36 days according to the sensitivity of the blood and cerebrospinal fluid culture. Phenobarbital was given at a loading dose of 20 mg/kg, then a maintenance dose of 5 mg/kg/day every 12 hours intravenously. Complication monitoring of the patient has performed ultrasonography with the...
result communicating hydrocephalus with ventriculitis. Symptoms monitoring consisted of vital signs, fluid balance, body weight, head circumference and symptom of increased intracranial pressure was measured daily.

After discharge, the patient has performed head computed tomography (CT) with the result of active communicating hydrocephalus. The patient planned to do surgery with the neurosurgical division.

**DISCUSSION**

Sepsis in the neonatal period has been proven to contribute to neonatal morbidity and mortality, and it is an ongoing major global public health challenge. Neonatal sepsis is systemic inflammatory response syndrome due to suspected or proven infection in a neonate. It is classified as early onset and late onset according to the times of the onset of findings. Early-onset neonatal sepsis is a clinical manifestation in the first three days of life. Late-onset sepsis is defined as sepsis occurring after three days of age. Neonatal sepsis varies from 6 to 9 cases per 1,000 live births but is higher among low-birth-weight neonates. Up to 20% of neonates are estimated to develop sepsis and approximately 1% die of sepsis-related causes. In this case, a patient with late-onset sepsis because sepsis occurs after three days of age.

Signs and symptoms of neonatal sepsis are not specific and involve multisystem; neurological (lethargy, seizure, poor tones), cardiopulmonary (respiratory distress, tachycardia or bradycardia), cyanosis, poor perfusion), gastrointestinal (vomiting, abdominal distention, feeding intolerance), hematologic (petechiae, hematemesis, melena) and metabolic (jaundice and temperature instability). Septic markers supporting neonatal sepsis are leukocytosis (>5x10^9/L), leukopenia (<5x10^9/L), thrombocytopenia (<150x10^9/L), IT ratio >0.2, procalcitonin >0.15 ng/ml, CRP ≥5 mg/dl and presence of toxic granule or vacuolization in blood smear. Positive blood culture is the gold standard for diagnosing sepsis. Cultures should be taken before the administration of antibiotics. Late-onset sepsis is due to microorganisms acquired from the environment after the delivery, nosocomial or community-acquired infections. Late-onset sepsis remains a major source of morbidity for preterm infants, resulting in high case-fatality rate, increased neonatal complications and impaired neurodevelopmental outcomes. Gram-positive bacteria are predominant in developed countries, while gram-negative organisms cause the majority of late-onset neonatal sepsis in developing countries.

Microorganisms in the genus Elizabethkingia are gram-negative, aerobic, pale yellow-pigmented, non-motile, glucose non-fermenting, non-spore-forming, oxidase-positive, weakly indole-positive and nitrate-negative bacilli. These bacteria are ubiquitously distributed in natural environments such as water, soils, fish, frogs, and insects, as well as in the tap water of hospitals. It is not considered a part of the normal human microflora. Elizabethkingia spp, isolates constitute a further threat, being able to thrive in aqueous environments and are associated with intravascular device-related bacteraemias, wound sepsis and ventilator-associated pneumonia under their ability to contaminate and persist in fluid-containing apparatus. Elizabethkingia meningoseptica has been found in the hospital environment in such sites as water supplies, the saline solution used for flushing procedures, disinfectants, and medical devices, including feeding tubes and arterial catheters. Elizabethkingia meningoseptica infections carry high morbidity and mortality rates and are associated with serious postinfectious sequelae, including hydrocephalus, deafness and developmental delay. In this case, the patient was 8 days old when first admitted to the hospital with sepsis symptoms, including fever, seizure, poor feeding, bulging of major fontanelle as along with laboratory result.
CASE REPORT

of thrombocytosis (572 x 10^9/μL), high IT Ratio (0.2), elevated CRP (49.30 mg/dL), blood smear examination revealed toxic granule, vacuolization of the leucocyte and reactive thrombocytosis. Elizabethkingia meningoseptica was isolated from blood culture, which convinced late-onset sepsis. Two of the patient’s siblings frequently handled the patient after playing with animals or soil, which could be the mediator of transmission of this pathogen.

Any newborn with bacterial sepsis is also at risk of meningitis. As such, the incidence of meningitis in neonatal sepsis has varied from 0.3-3% in various studies. However, late-onset sepsis has been reported to be fairly associated with meningitis, with a percentage ranging from 3 to 30%. Incidence of neonatal meningitis increased in developing countries by 0.8-6.1 per 1.000 live births. Meningitis in the neonatal period has a high morbidity rate, around 20% to 60%. Most organisms implicated in neonatal sepsis also cause neonatal meningitis. The clinical manifestations of neonatal meningitis can be subtle and not specific. Signs and symptoms of meningitis include temperature instability, lethargy, irritability, poor tone, seizures, feeding intolerance, vomiting, respiratory distress, apnea, or cyanotic episodes. There are several laboratory features in meningitis, including blood culture, complete blood count, IT ratio, procalcitonin, blood smear and lumbar puncture (LP) to examine cerebrospinal fluid (CSF), CSF culture, protein, glucose, and cell count. CSF pleocytosis is variable. Normal values range from 0-20/mm³ of which may be polymorphonuclear cells. Typically, neonates with meningitis have CSF glucose level <20-30 mg/dL and cerebrospinal fluid protein is usually elevated (>100-150 mg/dL). A definitive diagnosis of neonatal meningitis is a positive CSF culture. Of all neonates with positive blood culture results, only 30% showed positive culture CSF results. Of neonates with proven meningitis, 15-38% had a negative blood culture. Early neuroimaging by ultrasonography, magnetic resonance imaging (MRI), or computed tomography (CT) is indicated to assess the need for surgical intervention. Imaging should be repeated even after the antibiotic therapy has been completed, as there are reports of abscesses being identified weeks after the initiation of antibiotic therapy. In this case, patient symptoms were seizure, fever, poor feeding and bulging fontanelle was found on physical examination. Cerebrospinal fluid analysis revealed a cell number of 2520 cell/μL, mononuclear cell 20%, polymorphonuclear cell 80%, with Nonne and Pandy positive, protein level at 300 mg/dL, cerebrospinal fluid glucose level below 20 mg/dL and cerebrospinal fluid culture was isolated with Elizabethkingia meningoseptica.

Management of the patient with neonatal meningitis and late-onset sepsis, including emergency, definitive antibiotic, and supportive therapy. General supportive treatment includes oxygenation support, cardiovascular support and nutritional support. Treatment should be continued until 14 days after cultures are negative or for 21 days. For uncomplicated neonatal meningitis caused by gram-negative bacteria, a minimum of 21 days is recommended. Infants with repeated positive CSF cultures after initiating appropriate antibiotics are at risk for complications and poor outcomes. Generally, 3 days are required to sterilize the CSF in infants with gram-negative meningitis, whereas, in gram-positive meningitis, sterilization usually occurs within 36-48 hours. Follow-up of CSF examination is recommended until sterile CSF is documented. Elizabethkingia-related infections are complicated by the biofilm formation, intracellular invasion and multidrug resistance of the strains, and thus one needs to be cautious in selecting appropriate antimicrobial drugs. Elizabethkingia meningoseptica is resistant to multiple antibiotics that are typically prescribed for gram-negative bacterial infections, such as extended-spectrum β-lactam agents, aminoglycosides, tetracyclines and carbapenems due to intrinsic class A extended-spectrum β-lactamases (ESBLs) and inherent class B metallo-β-lactamases (MBLs). The antimicrobial susceptibility of Elizabethkingia may vary depending on the species as well as the region and time of bacterial isolation. However, the SENTRY antimicrobial surveillance program conducted from 1997 to 2001 showed that quinolones, rifampin, trimethoprim-sulfamethoxazole and piperacillin-tazobactam were the most active agents against Elizabethkingia meningoseptica. In this case, the patient was given antibiotics ampicillin and gentamicin with severe dose as empirical therapy. CSF evaluation on the second evaluation (10th day of severe dose antibiotic) revealed that the cell became decreased to 404 mm3, polymorphonuclear decrease to 35.7%, increasing total protein to 3770 mg/dL, CSF glucose 16 mg/dL, with improvement of CRP (3.8 mg/dL) and IT ratio (0.2). The blood culture revealed Elizabethkingia meningoseptica resistant to ampicillin. However, based on the clinical and septic marker improvement, we decided to continue the empirical antibiotics with severe doses by observing the clinical manifestation, septic marker evaluation, and CSF analysis. During the treatment, several inappropriate results were between clinical manifestation and laboratory results. On the third evaluation of the septic marker, the thrombocyte was increased, and on the third evaluation of cerebrospinal fluid analysis, protein increased. There was no improvement in the cell and glucose. With that consideration, the antibiotic was changed to levofloxacin according to the sensitivity of the blood and cerebrospinal fluid culture.

Early recognition of neonates at risk of poor prognosis would help provide management and treatment to improve outcomes and identify individuals who warrant early follow-up and intervention. Several risk factors associated with a poor clinical outcome of bacterial meningitis in children and adults have been identified in previous studies, including the presence of seizures, coma, hypotension, respiratory distress, hypoglycemia, leukopenia or thrombocytopenia and delay in the initiation of antibiotic therapy. Elizabethkingia meningoseptica infections carry high morbidity and mortality rates and are associated with serious postinfectious sequelae, including hydrocephalus, deafness, and developmental delay. In this case, the patient had low cerebrospinal fluid glucose concentrations and high
cerebrospinal fluid protein concentrations and the presence of seizures. The patient was at high risk of neurodevelopmental impairment and mortality.

Long-term complications in survivors are hearing loss, mental and motor disabilities including mental retardation, learning disabilities, behavioral problems, cerebral palsy, language disorders and impaired visual acuity. Neonatal meningitis can lead to severe consequences, including death or poor neurodevelopmental outcomes. Up to 50% of infants who survive neonatal meningitis develop some chronic neurologic sequelae, including seizures, cognitive deficits, cerebral palsy and hearing and visual impairment. Severe disability is reported in up to 25% of survivors. Monitoring neurodevelopmental outcomes, including cognitive development, neuropsychological performance and neurodevelopmental impairments (cerebral palsy, hearing deficit, and intellectual disability), must be evaluated periodically. In this case, the patient has performed ultrasonography, communicating hydrocephalus with ventriculitis. After discharge, the patient has performed head computed tomography (CT) with the result of active ventriculitis. After discharge, the patient has performed head computed tomography (CT) with the result of active ventriculitis. The patient planned to do surgery with the neurosurgical division.

CONCLUSION

A 14-day-old late preterm baby was assessed with late-onset neonatal sepsis and neonatal meningitis due to Elizabethkingia meningoseptica. The patient was given a severe dose of antibiotic ampicillin, gentamycin, and phenobarbital. However, the antibiotic was changed to levofloxacin for 36 days due to no improvement in the article except the patient's identity. This case report also has been considered the law according to the COPE regulations.

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None.

REFERENCES


Conflict of Interest

None.

Ethical Consideration

This case report has been permitted by the patient’s data will include in the article except the patient's identity. This case report has been considered the law according to the COPE regulations.

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