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CASE REPORT

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Emerging Infection with *Elizabethkingia meningoseptica* in Neonate. A Case Report

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Abstract

Background: *Elizabethkingia meningoseptica* are Gram-negative rod bacteria which are commonly found in the environment. The bacteria have also been associated with nosocomial infections, having been isolated on contaminated medical equipment, especially in neonatal wards.

Case report: Here, we present the case of a premature female infant born at 33 weeks' gestational age, with neonatal meningitis. The onset was marked by fever, in the 5th day of life, while in the Neonatal Intensive Care Unit. The patient was commenced on Gentamicin and Ampicillin, but her clinical condition worsened. Psychomotor agitation and food refusal developed in the 10th day of life, and a diagnosis of bacterial meningitis was made based on clinical and cerebrospinal fluid findings. A strain of *Elizabethkingia meningoseptica* sensitive to Vancomycin, Rifampicin and Clarithromycin was isolated from cerebrospinal fluid. First-line antibiotic therapy with Meropenem and Vancomycin was adjusted by replacing Meronem with Piperacillin/Tazobactam and Rifampicin. The patient's clinical condition improved, although some isolated febrile episodes were still present. The cerebrospinal fluid was normalized after 6 weeks of antibiotic treatment, although periventriculitis and tetraventricular hydrocephalus were revealed by imaging studies. Neurosurgical drainage was necessary.

Conclusion: *Elizabethkingia meningoseptica* can cause severe infection, with high risk of mortality and neurological sequelae in neonates. Intensive care and multidisciplinary interventions are crucial for case management.

Keywords: *Elizabethkingia meningoseptica*, neonatal meningitis, emergent infection, nosocomial

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Introduction

Elizabethkingia meningoseptica, assigned to the phyllum *Bacteroidaeota*, family *Flavobacteriaceae*, are Gram-negative aerobe rod, nonfermentative, nonmotile, nonspore-forming bacteria, which can be cultivated on blood and chocolate agar at 37^0C, and give positive reactions to catalase, oxidase and urease [1, 2]. The bacterial genus *Elizabethkingia* has been known as such since 2005 and was named after the American bacteriologist Elisabeth O. King, who in 1959 discovered *Flavobacterium meningoseptica*, which, until 1994, had been the previous name for *Elizabethkingia meningoseptica*. It was reclassified into the genus *Chryseobacterium (1994-2005)*, due to its production of a yellow pigment [3]. The genus *Elizabethkingia* includes four species: *E. anophelis, E. endophityca, E. miricola and E. meningoseptica* [4]. Based on genome sequence analysis, a recent report indicates the greater ability of *Elizabethkingia meningoseptica* to form biofilm, compared to other species [5]. *Elizabethkingia meningoseptica* are commonly found in soil and water, although it is also involved in hospital emergent infections related to contaminated medical equipment, especially in neonatal wards [3,6]. Elderly, newborns and immunocompromised patients are most susceptible to this infection, with recorded case-fatality rates of over 50% [7]. The diagnosis of *Elizabethkingia* infection is

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based on cultures from sterile sites, mostly from blood samples, although the prevalence of infection may be underestimated by misidentification. The Clinical and Laboratory Standards Institute does not have clinical breakpoints for *Elizabethkingia meningoseptica [8]*. New microbiological techniques, such as pulsed-field gel electrophoresis, the mass spectrometry method matrix-assisted laser desorption-ionisation time-of-flight mass spectrometry (MALDI-ToF) and optical mapping of the bacterial genome should improve bacterial diagnostics [9]. As the infection is prone to multidrug resistance, it is difficult to standardize treatment of *Elizabethkingia meningoseptica* infection. A review of medical literature confirms frequent inappropriate antibiotic use in *Elizabethkingia meningoseptica* infections and its subsequent influence on mortality risk [10,11].

Case report

A premature female infant born at 33 weeks' gestational age was admitted to the Neonatal Intensive Care Unit in the Pediatric Emergency Clinical Hospital in Galați, Romania, having been transferred from a secondary hospital when she was 2 weeks of age. The onset was marked by fever, in the 5th day after birth, while in the Neonatal Intensive Care Unit. Despite having antibiotic treatment with Ampicillin and Gentamicin, the clinical condition progressively worsened, as the patient presented with psychomotor agitation, food refusal and diarrhea.

The infant's history was unusual in that there was no medical control during the mother's pregnancy, there was a vaginal premature delivery, with a weight at birth of 2100 g, and an Apgar-Score of 9. Sociodemographic characteristics of the mother were as follows: from a rural area, minor age, minimal formal education, unemployed and unmarried.

The clinical examination at admission revealed: poor clinical condition, fever 40ºC, bulging fontanelle, general hypertonia with opisthotonus, abnormal Moro reflex, cardiac rate 170/min, respiratory rate 35-45/min, systolic murmur II-III, arterial blood pressure 75/40 mmHg, blood oxygen saturation 92%, chest wall retractions during respiratory movements. Significant biological findings revealed leukocytosis with neutrophilia, anemia, thrombocytosis, positive D-Dimer, elevation of inflammatory markers and serum lactate dehydrogenase. Chest X-ray, transfontanellar and abdominal ultrasound were normal. Clinical suspicion of neonatal sepsis with meningoencephalitis was confirmed by the biochemical and cytological findings of the cerebrospinal fluid (CSF) (Table 1).

Table 1. Successive Characteristics of Biological Data in a neonate sepsis with E. meningoseptica

	Normal	Paediatric Clinic Hospital Galati				
		Day 1	Day 14	Day 21	Day 28	Day 42
Cerebrospinal fluid						
Appearance	clear	deposits	turbid	turbid	clear	clear
Leukocyte [/mm^3]	1-10	605	96	218	34	8
PMN [%]	0	95	60	58	10	0
Proteins [mg/dl]	12-60	620	178	218	114	67
Glucose [mg/dl]	40-70	<20	21.8	<20	35.3	45
Chloride [mg/dl]	7.15-7.45	6.31	7.08	6.73	7.19	7.20
Blood						
WBC [x10^3/mm^3]	6-17	20300	21000	20200	9900	8300
Neutrophils [%]	20-40	53	66	54	25.4	22.4
Thrombocytes [x10^3/mm^3]	220-520	953	784	605	482	473
Fibrinogen [mg/dl]	150-400	1600	848	724	337.5	296
Glycemia [mg/dl]	65-110	109.8	82.3	60.9	73	81
ALT [IU/l]	14-36	30	154	44	76	49
AST [IU/l]	9-52	26	111	46	39	28
LDH [IU/l]	225-600	783	1034	1009	842	640

A strain of *Elizabethkingia meningoseptica* was isolated in the CSF and in the blood culture by a VITEK 2 system. In vitro antibiotic activity testing found: Vancomycin-sensitive, Rifampicin -sensitive and Clarithromycin - sensitive, Ciprofloxacin - low resistance, Ampicillin - resistant, Cephepime - resistant, Ceftazidime - resistant, Cefuroxime - resistant, Trimethoprim -Sulphamethoxazol - resistant, Penicillin G - resistant, Methicillin - resistant. Neonatal bacterial meningitis with probable nosocomial origin showed an apparent clinical and CSF improvement during the first two weeks, under antibiotic treatment with Vancomycin and Meropenem. However, several "spikes" in the temperature chart, less than 39^0C, had been recorded and regression of CSF pathological changes were suboptimal in the 14th day (Table 1, Table 2).

Alerts were generated for poor outcomes, and antibiotic treatment was adjusted by replacing Meropenem with Rifampicin, while continuing Vancomycin. Piperacillin/tazobactam was added on the 21st day, due to recrudescence of CSF pathological changes. Periventriculitis and tetraventricular hydrocephaly were revealed on the 4th week by transfontanellar ultrasound and were confirmed by magnetic resonance imaging.

The cerebrospinal fluid normalized in 6 weeks, suggesting a positive response from Piperacillin/tazobactam.

The infant was referred to a neurosurgeon for CSF drainage and required neuropsychiatric monitoring for late complications. Epidemiological investigation classified the infection as an isolated case. No source of infection was identified.

Additional specific intensive care interventions contributed to case management, including supplemental oxygen with high-flow nasal cannula, intravenous hydrocortisone infusion, fluid and electrolyte therapy, albumin therapy, diuretics, antiplatelet aggregation with dipyridamole.

DISCUSSION

The main clinical characteristic of neonatal bacterial meningitis is the high frequency of nonspecific symptoms, including irritability, poor feeding, hypertonia and concomitant septic shock in more than 25% of cases, as we have found in the presented case study [12]. The most common pathogens related to neonatal meningitis are *Streptococcus agalactiae* and *Escherichia coli*, appearing in two thirds of cases [12,13]. The antibiotic combination therapy of Ampicillin plus Cefotaxime or Ampicillin plus an aminoglycoside is recommended as empirical treatment for neonatal meningitis and was considered the first-line antibiotic therapy while the patient was in our Neonatal Intensive Care Unit [12,13,14].

Elizabethkingia meningoseptica is a rare cause of meningitis in newborns, mostly associated with premature birth. However, meningitis is the most common infection associated with *Elizabethkingia meningoseptica*. Cases of endocarditis, pneumonia, cellulitis, wound infections, bacteremia following burns, abdominal abscesses, dialysis-associated peritonitis or endophthalmitis, especially in immunocompromised patients, have also been reported [15,16,17,18]. The impact of *Elizabethkingia meningoseptica* in susceptible hosts, whether by simple colonization or invasive infections, suggests the influence of the immune response on a variety of pathogenic mechanisms [16]. The sources of infection could not be accurately identified in most reported symptomatic cases, although nosocomial transmission was usually presumed [16,17].

The antibiotic profile of *Elizabethkingia meningoseptica* is different from other Gram-negative rods. Namely, the bacterium is characterized by its inherent resistance to aminoglycosides, β-lactam agents, Chloramphenicol and carbapenems, but also by its susceptibility to Rifampicin, Ciprofloxacin, Vancomycin and Trimethoprim–Sulfamethoxazole [17,19]. The significance of *Elizabethkingia meningoseptica* antibiotic sus-

Table 2. Sequential antibiotic treatment

Antibiotic treatment	Week 1	Week 2	Week 3	Week 4	Week 5	Week 2
Ampicillin +Gentamicine	⇩					
Meropenem		⇩	⇩			
Vancomycine		⇩	⇩	⇩	⇩	⇩
Rifampicine			⇩	⇩	⇩	⇩
Piperacillin/Tazobactam				⇩	⇩	⇩

ceptibility is limited, as there are no available validated susceptibility testing methods or antimicrobial treatment guidelines [20]. Our bacterial isolate was sensitive to Vancomycin, but the clinical and CSF outcomes were below expectations. According to a review of medical literature, Vancomycin has been recommended for the treatment of meningitis with *Elizabethkingia meningoseptica, but* the efficacy has been questioned in several recent studies, with regards to the high minimum inhibitory concentration [19,21]. Additionally, successful use of Piperacillin/tazobactam was documented by clinical reports [1, 21]. Considering these arguments, we decided to escalate the antibiotic treatment by adding rifampicin and Piperacillin/tazobactam, although Piperacillin was not considered in our antibiotic testing.

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 [22]. 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 [22,23]. Piperacillin/tazobactam has a lower concentration in the cerebrospinal fluid compared to levofloxacin [24]. However, we avoided fluoroquinolone because of the low susceptibility for Ciprofloxacin of our *Elizabethkingia meningoseptica* strain, as well as the relative lack of data available on the safety and efficacy of levofloxacin in neonates [25].

Normalization of CSF was achieved in the present case after six weeks, but hydrocephaly developed, and other late neuropsychological complications are possible over the next several years. This outcome is confirmed in the literature review which showed 57% mortality rate and 69% hydrocephaly rate in survivors [21,26,27].

Conclusions

Elizabethkingia meningoseptica is an emerging infection and a nosocomial threat, with high risk for complications and mortality in premature neonates. The improvement of accuracy in bacterial identification and standardization of antibiotic susceptibility tests are essential for early diagnostic and etiologic treatment, in order to reduce mortality and neurological complications. Intensive care procedures and multidisciplinary interventions are crucial for case management. Active infection control in hospital environments, especially of water sources, is necessary to prevent *Elizabethkingia meningoseptica* epidemics.

Conflict of interest

None to declare.

References

1. Bhat KS, Priya R, Krishnan L, Kanungo R. Elizabethkingia meningoseptica bacteremia in a neonate: A case report and mini-review of the literature. J Curr Res Sci Med. 2016;2:42-5.
2. Oren A, da Costa MS, Garrity GM, et al. Proposal to include the rank of phylum in the international code of nomenclature of prokaryotes. Int J Syst Evol Microbiol. 2015;65:4284–7.
3. Kim KK, Kim MK, Lim JH, Park HY, Lee ST. Transfer of *Chryseobacterium meningosepticum* and *Chryseobacterium miricola* to *Elizabethkingia* gen. nov. as *Elizabethkingia meningoseptica* comb. nov. and *Elizabethkingia miricola* comb. nov. Int J Syst Evol Microbiol. 2005;55(Pt 3):1287–93.
4. Breurec S, Criscuolo A, Diancourt L, et al. Genomic epidemiology and global diversity of the emerging bacterial pathogen *Elizabethkingia anophelis*. Sci Rep. 2016, 6:30379.
5. Chen S, Soehnlen M , Downes FP, Walker ED. Insights from the draft genome into the pathogenicity of a clinical isolate of *Elizabethkingia meningoseptica* Em3. Stand Genom Sci. 2017;12:56.
6. Jean SS, Lee WS, Chen FL, Ou TY, Hsueh PR. *Elizabethkingia meningoseptica*: an important emerging pathogen causing healthcare-associated infections. J Hosp Infect. 2014;86(4):244–9.
7. Pereira GH, Garcia DO, Abboud CS, Barbosa VLB, da PSL S. Nosocomial infections caused by *Elizabethkingia meningoseptica*: an emergent pathogen. Braz J Infect Dis. 2013;17:606–9.
8. CLSI. Performance Standards for Antimicrobial Susceptibility Testing. 28th ed. CLSI supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2018.
9. Eriksen HB, Gumpert H, Faurholt CH, Westh H. Determination of *Elizabethkingia* Diversity by MALDI-TOF Mass Spectrometry and Whole-Genome Sequencing. Emerg Infect Dis. 2017;23(2):320-3.
10. Hsu MS, Liao CH, Huang YT, et al. Clinical features, antimicrobial susceptibilities, and outcomes of *Elizabethkingia meningoseptica* (*Chryseobacterium meningosepticum*) bacteremia at a medical center in Taiwan, 1999–2006. Eur J Clin Microbiol Infect Dis. 2011;30(10):1271–8.
11. Lin PY, Chen HL, Huang CT, Su LH, Chiu CH. Biofilm production, use of intravascular indwelling catheters and inappropriate antimicrobial therapy as predictors of fatality

in ***Chryseobacterium meningosepticum*** bacteraemia**.** Int J Antimicrob Agents. 2010;36:436–40.

12. van de Beek D, Cabellos C, Dzupova O, et al. ESCMID guideline: Diagnosis and treatment of acute bacterial meningitis for the ESCMID Study Group for Infections of the Brain (ESGIB). Clin Microbiol Infect. 2016;22:S37-S62.
13. Tunkel AR, Hartman BJ, Kaplan SL, et al. Practice Guidelines for Bacterial Meningitis. ***Clin Infect Dis.*** 2004;39:1267-84.
14. Brouwer MC, Tunkel AR, van de Beek D. Epidemiology, diagnosis, and antimicrobial treatment of acute bacterial meningitis. Clin Microbiol Rev. 2010;23(3):467–92.
15. Hsu MS, Liao CH, Huang YT, et al. Clinical features, antimicrobial susceptibilities, and outcomes of ***Elizabethkingia meningoseptica (Chryseobacterium meningosepticum)*** bacteremia at a medical center in Taiwan, 1999–2006. Eur J Clin Microbiol Infect Dis. 2011;30(10):1271–8.
16. Ceyhan M, Celik M. ***Elizabethkingia meningosepticum (Chryseobacterium meningosepticum)*** Infections in Children. Int J Pediatr. 2011:215-37.
17. Shah Z, Soodhana D, Kalathia M, Parikh Y. ***Elizabethkingia meningoseptica***: an emerging threat. Int J Contemp Pediatr. 2017;4(5):1909-10.
18. Kavuncuoglu S, Gursoy S, Turel O, Aldemir EY, Hosaf E. Neonatal bacterial meningitis in Turkey: epidemiology, risk factors, and prognosis. J Infect Dev Ctries. 2013;7(2):73–81.
19. Lin PY, Chu C, Su LH, Huang CT, Chang WY, Chiu CH. Clinical and microbiological analysis of bloodstream infections caused by ***Chryseobacterium meningo-septicum*** in nonneonatal patients. J Clin Microbiol. 2004;42(7):3353–5.
20. Shinha T, Ahuja R. Bacteremia due to ***Elizabethkingia meningoseptica***. IDcases. 2015;2(1):13-5.
21. Issack MI, Neetoo Y. An outbreak of ***Elizabethkingia meningoseptica*** neonatal meningitis in Mauritius. J Infect Dev Ctries. 2011;5(12):834–39.
22. Huang YC, Lin YT, Wang FD. Comparison of the therapeutic efficacy of fluoroquinolone and non-fluoroquinolone treatment in patients with ***Elizabethkingia meningoseptica*** bacteraemia. Int J Antimicrob Agents. 2018;51(1):47-51.
23. Vincent JL, Bassetti M, Francois B, et al. Advances in antibiotic therapy in the critically ill. Crit Care. 2016; 20:133.
24. Neuner EA, Ahrens CL, Groszek JJ, et al. Use of therapeutic drug monitoring to treat ***Elizabethkingia meningoseptica*** meningitis and bacteraemia in an adult. J Antimicrob Chemother. 2012;67:1558–60.
25. Newby BD, Timberlake KE, Lepp LM, Mihic T, Dersch-Mills DA. Levofloxacin Use in the Neonate: A Case Series. JPPT. 2017;22(4):304-13.
26. Bruun B, Tversrupjensen E, Lundstrom K, Andersen GE. The ***C meningosepticum*** infection in a Neonatal ward. Eur J Clin Microbiol Infect Dis. 1989;816:509-14.
27. Bloch KC, Nadarajah R, Jacobs R. ***Chryseobacterium meningosepticum***: an emerging pathogen among immunocompromised adults. Report of 6 cases and literature review. Medicine (Baltimore), 1997;76: 30-41.