**Elizabethkingia meningoseptica (Chryseobacterium meningosepticum)** bacteraemia: a series of 12 cases at Prince Sultan Military Medical City KSA

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**Abstract**

The aim of this study was to describe the epidemiological data, clinical features and outcome of patients with *Elizabethkingia meningoseptica* bacteraemia and to report the antimicrobial susceptibility pattern. All patients with *E. meningoseptica* bacteraemia were retrospectively recruited at the Prince Sultan Military Medical City, Riyadh, Saudi Arabia, between June 2013 and May 2019. Epidemiological data, clinical features and patient outcome, as well as antimicrobial susceptibilities of *E. meningoseptica*, were collected from patient electronic medical records. Twelve patients (eight male and four female) with *E. meningoseptica* bacteraemia were included in the study. Eleven patients acquired the infection from the hospital, five of whom were in the intensive care unit. All patients had one or more underlying medical conditions or interventions, including chronic illness (eight cases), major surgery (three cases), pulmonary fibrosis (one case), sickle-cell anaemia (one case) and end-stage renal disease (one patient on haemodialysis). Eleven patients had a prolonged stay in the hospital (≥3 months), and nine patients had received prolonged antibiotic therapy. Three patients had polymicrobial bacteraemia, including *Serratia marcescens* (two cases) and *Enterococcus faecalis* (one case). All *E. meningoseptica* isolates were susceptible to trimethoprim/sulfamethoxazole, piperacillin/tazobactam and moxifloxacin but showed a high degree of resistance to β-lactam antibiotics, aminoglycosides and carbapenems. These findings have important implications for the clinician selecting optimal antimicrobial regimens for patients with risk factors for *E. meningoseptica* infection.

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**Keywords:** Antibiotic resistance, bacteraemia, *Elizabethkingia meningoseptica*, polymicrobial bacteraemia, prognosis

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**Introduction**

*Elizabethkingia meningoseptica* (*Chryseobacterium meningosepticum*), previously known as *Flavobacterium meningosepticum*, is a rod-shaped gram-negative bacterium widely distributed in nature (e.g., in water, plants and soil). Many environmental studies have shown that *E. meningoseptica* can survive in chlorine-treated municipal water supplies, often colonizing sink basins and taps, and has become a potential reservoir for infections in the hospital environment. The organisms have been recovered from dialysis systems, pharmaceuticals, and medical devices (including intravascular catheters, respirators and intubation tubes) [1,2]. *E. meningoseptica* is commonly isolated from clinical specimens, and is an uncommon pathogen causing neonatal meningitis, pneumonia, bacteraemia, sepsis, soft-tissue infections and other infections, primarily in immunocompromised patients. It has also been reported to cause outbreaks in neonatal and adult intensive care units (ICUs) [2,3]. The majority of cases have been hospital-acquired infections, and most of the patients had underlying conditions such as neoplasia, diabetes mellitus and cardiovascular disease [4].

*E. meningoseptica* is resistant to multiple antibiotics that are typically prescribed for gram-negative bacterial infections, such as extended-spectrum β-lactam agents and aminoglycosides [5,6].
Most of the reported cases have originated in Taiwan, with relatively few cases published from India, Australia, Europe and the United States; no case has as yet been reported in Saudi Arabia. The aim of this study was therefore to report epidemiological data, clinical features, antimicrobial susceptibility and outcomes of patients with E. meningoseptica bacteremia at the Prince Sultan Military Medical City (PSMMC), Riyadh, Saudi Arabia.

Materials and methods

All patients with a positive blood culture of E. meningoseptica admitted to the PSMMC between June 2013 and May 2019 were retrospectively included in this study. Demographic data, clinical diagnosis, outcome and antimicrobial susceptibilities for all isolates were extracted from patients’ electronic medical records. Primary identification of E. meningoseptica was based on conventional culture techniques of clinical samples. Suspected colonies were then identified using manual or automated phenotypic methods, namely, manual biochemical reactions using the API 20 NE identification system for non-fastidious, non-enteric gram-negative rods (bioMérieux, Marcy l’Etoile, France) or the automated MicroScan WalkAway system with the conventional dried gram-negative identification panel Neg Breakpoint Combo50 (Beckman Coulter, South Kraemer Boulevard Brea, California, USA). Susceptibility testing was performed for all isolates to determine either the breakpoint or the MIC of the antimicrobials tested. Breakpoint was determined using the MicroScan WalkAway system with the conventional dried gram-negative identification panel Neg Breakpoint Combo50 panel for identification, and ETEST strips (bioMérieux, Marcy l’Etoile, France) were used for MIC determination.

Definitions

An episode of significant bacteremia was defined as the identification of at least one blood culture positive for E. meningoseptica. Polymicrobial bacteremia was defined as the presence of bacteria or yeasts in addition to E. meningoseptica in the blood culture. Recent surgery was defined as a surgical procedure performed within 1 month prior to the positive blood culture of E. meningoseptica. Appropriate antibiotic therapy was defined as the use of at least one antibiotic to which E. meningoseptica was susceptible according to susceptibility testing. Death related to bacteremia was considered if the patient died <28 days after the onset of bacteremia and if no other cause of death was identified.

Results

Between June 2013 and May 2019, clinical isolates from 12 patients with E. meningoseptica bacteremia were collected. The clinical characteristics of the 12 patients are summarized in Table 1. Eleven patients acquired the infection from the hospital; five of them were in the ICU. All the patients had one or more underlying illnesses, including chronic illness (eight cases), major surgery (three cases), pulmonary fibrosis (one case), sickle-cell anaemia (one case) and end-stage renal disease (one patient on haemodialysis). All patients had prolonged stay in the hospital (≥3 months), and nine of them had received prolonged antibiotic treatment (≥2 weeks) prior to having a positive blood culture. Three patients had polymicrobial bacteremia, including two cases with Serratia marcescens (case numbers 2 and 7) and one case with Enterococcus faecalis (case number 1). The clinical diagnosis was central-line-associated bloodstream infection (CLABSI) in four cases, primary isolated bacteremia and ventilator-associated pneumonia (VAP) in three cases each, and septic shock in two cases. Initially, only one patient (case number 9) received appropriate empirical antibiotic therapy after blood culture results and susceptibility tests, in five cases empirical antibiotics were adjusted to appropriate prescription, and for the remaining cases inappropriate treatment was maintained. Despite the high number of patients receiving inappropriate treatment, only two died within 28 days after the onset of bacteremia. Both deaths were unrelated to the infection; one was due to severe VAP with advanced pulmonary fibrosis (case number 5), and the other was due to heart failure while the patient’s blood culture was negative (case number 8).

Regarding susceptibility testing (Table 2), all isolates were susceptible to trimethoprim/sulfamethoxazole, piperacillin/tazobactam and moxifloxacin. The susceptibility to levofloxacin and ciprofloxacin was 92% and 58.3%, respectively. All E. meningoseptica isolates showed resistance to amikacin, gentamycin, ceftriaxone, imipenem and meropenem.

Discussion

E. meningoseptica has been found in the hospital environment in such sites as water supplies, saline solution used for flushing procedures, disinfectants, and medical devices (including feeding tubes and arterial catheters). To the best of our knowledge, this is the first study to describe the clinical features, antimicrobial susceptibilities and outcomes of E. meningoseptica bacteremia in the Arabian Gulf. In previous studies, neonatal patients, especially those that were premature, were at great risk for E. meningoseptica infection [3]. In the present study, however, only one patient was a neonate and most of the patients were adults.

In the past decade, it has been observed that the number of patients with E. meningoseptica bacteremia is increasing;
TABLE 1. Clinical characteristics and outcomes of patient with Elizabethkingia meningoseptica bacteraemia

| Case No. | Age (y, mo, d)/gender | Location         | Underlying and other associated condition(s) | Clinical diagnosis | Polymicrobial infection | Empirical antibiotic | Therapeutic antibiotic | Outcome        |
|----------|-----------------------|------------------|-----------------------------------------------|-------------------|------------------------|---------------------|------------------------|---------------------|
| 1        | 15 y/M                | Medical ward     | Sickle-cell anaemia, CVC, prolonged stay      | CLABSI            | Yes                    | Enterococcus faecalis | Ceftriaxone + azithromycin | Recovered       |
| 2        | 9 mo/M                | NICU             | Abdominal and cardiac surgery, CVC, ventilator, prolonged stay, ICU admission | CLABSI,          | Yes                    | Stenotrophomonas spp   | Meropenem + vancomycin     | Recovered       |
| 3        | 12 d/M                | NICU             | Tracheo-oesophageal surgery, ventilator, prolonged stay, ICU admission | VAP              | No                     | Meropenem + vancomycin     | Vancomycin + tazocin     | Recovered       |
| 4        | 90 y/M                | Medical ward     | CVA, CHF, DM, HTN, CVC, prolonged ABX use, prolonged stay | CLABSI            | No                     | Meropenem               | Bactrim                | Recovered       |
| 5        | 43 y/M                | GICU             | Quadriplegia, chest fibrosis, ventilator, prolonged ABX use, prolonged stay, ICU admission | VAP              | No                     | Meropenem + vancomycin     | Meropenem + vancomycin     | Died after 8 days |
| 6        | 2 y/F                 | PICU             | Congenital central hypopventilation syndrome, ventilator, prolonged ABX use, prolonged stay, ICU admission | VAP              | No                     | Meropenem + vancomycin     | Meropenem + vancomycin     | Recovered       |
| 7        | 90 y/M                | GICU             | Bowel ischaemia, parkinsonism, DM, HTN, CVA, prolonged ABX use, prolonged stay, ICU admission | Septic shock     | Yes                    | Stenotrophomonas spp   | Meropenem + Tazocin       | Recovered       |
| 8        | 98 y/F                | Medical ward     | HF, prolonged ABX use, prolonged stay         | Bacteraemia       | No                     | Gentamycin             | Bactrim                | Died after 25 days   |
| 9        | 91 y/F                | Medical ward     | DM, HF, ESRO, prolonged ABX use, prolonged stay | Bacteraemia       | No                     | Tazocin               | Tazocin                | Recovered       |
| 10       | 102 y/F               | Medical ward     | Prolonged ABX use, prolonged stay             | Septic shock     | No                     | Meropenem              | Meropenem              | Recovered       |
| 11       | 64 y/M                | Medical ward     | CVA, ventilator, prolonged ABX use, prolonged stay | Bacteraemia,     | No                     | Meropenem              | Meropenem              | Recovered       |
| 12       | 46 y/M                | Nephrology ward  | CKD, CVC, prolonged ABX use, prolonged stay   | Elizabethkingia meningoseptica | No                     | Vancomycin             | Ciprofloxacin         | Recovered       |

DM, diabetes mellitus; ABX, antibiotic; HTN, hypertension; HF, heart failure; CHF, congestive heart failure; CKD, chronic kidney disease; ESRO, end-stage kidney disease; CVA, cerebrovascular accident; ICU, intensive care unit; CVC, central venous catheter; CLABSI, central-line-associated bloodstream infection; VAP, ventilator-associated pneumonia; NICU, neonatal intensive care unit; PICU, paediatric intensive care unit; GICU, general intensive care unit; CPICU, cardiac paediatric intensive care unit.

Indeed, at a medical centre in Taiwan, the incidence (per 100,000 admissions) of *E. meningoseptica* bacteraemia increased from 7.5 in 1996 to 35.6 in 2006 [7]. Despite many authors reporting an increase in bacteraemia due to *E. meningoseptica* outbreaks [7,8], the incidence of *E. meningoseptica* bacteraemia in the present series was not associated with a hospital outbreak. This may be because of successful implementation of infection control programmes in our hospital, such as care bundles for CLABSI and VAP, isolation precautions, and a hand hygiene programme.

*E. meningoseptica* bacteraemia in humans is usually acquired in the hospital and is most likely associated with the presence of invasive equipment such as intravascular catheters, endotracheal tubes and prosthetic devices, treatment with long-term broad-spectrum antibiotics, or long periods of hospitalization [7–9]. The current study showed that patients with severely debilitating diseases, patients who had undergone various invasive procedures or ICU admission, and patients who had received antibiotics during a long period of hospitalization were at high risk for bacteraemia caused by *E. meningoseptica*.

In our study, patients with intravascular-catheter-related bacteraemia caused by *E. meningoseptica* improved clinically while the catheter remained in place, even though two of four patients with intravascular catheters received inappropriate antibiotics. This result is in accord with findings reported by Hsu et al. [7] suggesting that intravascular-catheter-related bacteraemia caused by *E. meningoseptica* does not usually require removal of the catheter.

Previous studies revealed a cumulative mortality rate of 52% in neonates and 33% in non-neonates with *E. meningoseptica* infections [1]. In the largest series of 118 patients with *E. meningoseptica* bacteraemia at a medical centre in Taiwan, the 14-day mortality rate was 23% [7]. Acquisition of the infection in an ICU was a significant predictor of mortality. These results all support previous findings by Lin et al. that host factors were the critical determinant in predicting outcomes [10]. In our series, despite most of patients not receiving appropriate antibiotic treatment, mortality rate was low (16.5%) and only two patients died within 28 days, which was much lower than that reported in past studies [1,7]. In addition, both of the deaths in this study were unrelated to the infection; one was due to severe VAP with advanced pulmonary fibrosis (case number 5), and the other was due to heart failure while the patient’s blood culture was negative.

In general, polymicrobial bacteraemia accounts for 5–20% of bloodstream infections, and patients often have underlying medical conditions (e.g. malignancy, neutropenia, gastrointestinal disease and genitourinary disease) or interventions (e.g. anticoagulants or chemotherapy) [10].
TABLE 2. Result of antimicrobial susceptibility testing

| Antibiotic               | 1  | 2  | 3  | 4  | 5  | 6  | 7  | 8  | 9  | 10 | 11 | 12 |
|--------------------------|----|----|----|----|----|----|----|----|----|----|----|----|
| Amikacin                 | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  |
| Gentamicin               | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  |
| Ceftazidime              | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  |
| Ciprofloxacin            | R  | R  | S  | S  | S  | S  | S  | S  | R  | S  | S  | S  |
| Ceftriaxone              | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  | S  | S  |
| Imipenem                 | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  |
| Levofloxacin             | S  | S  | S  | S  | S  | S  | S  | S  | S  | S  | S  | S  |
| Meropenem                | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  |
| Trimethoprim/sulfamethoxazole (Bactrim) | S  | S  | S  | S  | S  | S  | S  | S  | S  | S  | S  | S  |
| Piperacillin/tazobactam (tazocin) | S  | S  | S  | S  | S  | S  | S  | S  | S  | S  | S  | S  |
| Colistin                 | R  | R  | R  | R  | R  | R  | R  | R  | S  | R  | R  | R  |
| Tetracycline             | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  | R  |
| Moxifloxacin             | S  | S  | S  | S  | S  | S  | S  | S  | S  | S  | S  | S  |

R, resistant; S, susceptible.

Recent surgical procedures and the presence of central venous catheters. Polymicrobial bacteraemia is associated with a worse outcome [11], and the detection of other organisms in the sample poses a dilemma for clinicians. In the series of Hsu et al., 45 patients (38.1%) had concomitant pathogens in blood cultures, including ten patients with Acinetobacter baumannii, nine patients with methicillin-resistant Staphylococcus aureus, and five patients with Pseudomonas aeruginosa [7]. In the current study, polymicrobial bacteraemia occurred in 25% of the patients (three cases), and all of these patients had underlying medical conditions or interventions including diabetes mellitus, recent surgery, central venous catheters and prolonged hospital stay. These patients were treated with effective antibiotics for concomitant infection (Serratia marcescens, Enterococcus faecalis), but only one patient received appropriate treatment for both bacteria. The favourable prognosis and outcome of all these patients can be explained by the appropriate treatment given to the second infecting organisms, and raises questions regarding the pathogenicity of E. meningoseptica.

The choice of optimal antibiotic agents for treating E. meningoseptica infection is difficult because of the unpredictability and breadth of antimicrobial resistance of this organism which often exhibits resistance to antibiotics prescribed to treat serious gram-negative bacteria, such as β-lactam agents, aminoglycosides and carbapenems [12]. Lin et al. reported that 54.5% of patients infected with E. meningoseptica bacteraemia recovered without receiving appropriate antibiotic treatment [10]. In our study, among six patients who received inappropriate antibiotic for E. meningoseptica bacteraemia, five of them recovered. This improvement may be attributable to the low virulence of E. meningoseptica. However, further studies are required to understand the virulence mechanisms of E. meningoseptica.

With regard to antimicrobial susceptibility, our findings were similar to those reported in most studies [13–15], with E. meningoseptica showing resistance to carbapenems, aminoglycosides and β-lactam antibiotics, and sensitivity to fluoroquinolones, piperacillin/tazobactam and trimethoprim/sulfamethoxazole. This resistance pattern may be related to prolonged courses of antibiotics in these patients, which might lead to selective pressure for resistance in this organism.

The present study has several limitations. It was a retrospective study, and missing data might have concealed potential risk factors that were not documented in the medical records. In addition, our sample size was small. However, a prospective study with a significant number of patients would require a study duration of many years. The implementation of strict methods for infection control in the study institution, such as care bundles for CLABSI and VAP, might have influenced the prevalence of E. meningoseptica infections in this study. In addition, the pathogenicity, antimicrobial susceptibility and virulence factors of E. meningoseptica remain unclear. To address these limitations, a well-designed prospective study may be necessary in the future.

**Conclusion**

In summary, our study indicates that patients with predisposing factors—such as severe debilitating conditions, ICU admission, indwelling devices, prolonged antibiotic treatment and long periods of hospitalization—are at greater risk of developing E. meningoseptica bacteraemia. The resistance of this organism to multiple antibiotics, including carbapenems, aminoglycosides and β-lactam agents, makes it difficult to determine optimal therapeutic approaches. The relatively low mortality rate and the clinical improvement among patients with E. meningoseptica bacteraemia despite not receiving the appropriate antibiotics are not fully understood. Further cases should be evaluated and
a study on the pathogenicity of this organism in humans conducted to elucidate these phenomena.

Conflict of interest

No conflict of interest.

References

[1] Bloch KC, Nadarajah R, Jacobs R. Chryseobacterium meningosepticum: an emerging pathogen among immunocompromised adults. Medicine 1997;76:30–41.
[2] 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.
[3] Chiu CH, Waddington M, Greenberg D, Schreckenberger PC, Carnahan AM. Atypical Chryseobacterium meningosepticum and meningitis and sepsis in newborns and the immunocompromised. Taiwan. Emerg Infect Dis 2000;6(5):481–6.
[4] Lin JN, Lai CH, Yang CH, Huang YH. Elizabethkingia infections in humans: from genomics to clinics. Microorganisms 2019;28(9): pii: E295.
[5] Hung PP, Lin YH, Lin CF, Liu MF, Shi ZY. Chryseobacterium meningosepticum infection: antibiotic susceptibility and risk factors for mortality. J Microbiol Immunol Infect 2008;41(2):137–44.
[6] Bolash NK, Liu HH. Quinolone susceptibility of multi resistant Flavobacterium meningosepticum clinical isolates in one urban hospital. Drugs 1995;49:168–70.
[7] Hsu MS, Liao CH, Huang YT, Liu CY, Yang CJ, Kao KL, 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 Micro Infect Dis 2011;30(10):1271–8.
[8] Tai IC, Liu TP, Chen YJ, Lien RI, Lee CY, Huang YC. Outbreak of Elizabethkingia meningoseptica sepsis with meningitis in a well-baby nursery. J Hosp Infect 2017;96(2):168–71.
[9] Dias M, Prashant K, Pai R, Scaria B. Chryseobacterium meningosepticum bacteremia in diabetic nephropathy patient on hemodialysis. Indian J Nephrol 2010;20(4):203.
[10] Lin PF, Chu C, Su LH, Huang CT, Chang WY, Chiu CH. Clinical and microbiological analysis of bloodstream infections caused by Chryseobacterium meningosepticum in non-neonatal patients. J Clin Microbiol 2004;42(7):3353–5.
[11] Khatib R, Sharma M, Johnson LB, Riederer K, Briski L. Polymicrobial Staphylococcus aureus bacteremia: frequency, distinguishing characteristics and outcome. Diagn Microbiol Infect Dis 2016;86(3):311–5.
[12] Chang JC, Hsueh PR, Wu JJ, Ho SW, Hsieh WC, Luh KT. Antimicrobial susceptibility of flavobacteria as determined by agar dilution and disk diffusion methods. Antimicrob Agents Chemother 1997;41(6):1301–6.
[13] Kirby JT, Sader HS, Walsh TR, Jones RN. Antimicrobial susceptibility and epidemiology of a worldwide collection of Chryseobacterium spp: report from the SENTRY Antimicrobial Surveillance Program (1997–2001). J Clin Microbiol 2004;42(1):445–8.
[14] Jean SS, Hsieh TC, Ning YZ, Hsueh PR. Role of vancomycin in the treatment of bacteraemia and meningitis caused by Elizabethkingia meningoseptica. Int J Antimicrob Ag 2017;50(4):507–11.
[15] Huang YC, Huang YW, Lin YT, Wang FD, Chan YJ, Yang TC. Risk factors and outcome of levofloxacin-resistant Elizabethkingia meningoseptica bacteremia in adult patients in Taiwan. Eur J Clin Microbiol Infect Dis 2017;36(8):1373–80.