

# *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 ( $\geq 3$  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  $\beta$ -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  $\beta$ -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* bacteraemia 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 Neg Breakpoint Combo50 panel for identification, and ETEST strips (bioMérieux, Marcy l'Etoile, France) were used for MIC determination.

## Definitions

An episode of significant bacteraemia was defined as the identification of at least one blood culture positive for *E. meningoseptica*. Polymicrobial bacteraemia 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 bacteraemia was considered if the patient died  $\leq 28$  days after the onset of bacteraemia and if no other cause of death was identified.

## Results

Between June 2013 and May 2019, clinical isolates from 12 patients with *E. meningoseptica* bacteraemia 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 with end-stage renal disease (one patient on haemodialysis). All patients had prolonged stay in the hospital ( $\geq 3$  months), and nine of them had received prolonged antibiotic treatment ( $\geq 2$  weeks) prior to having a positive blood culture. Three patients had polymicrobial bacteraemia, 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 bacteraemia 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 bacteraemia. Both of the 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* bacteraemia 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* bacteraemia 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	Ceftriaxone + amoxicillin	Recovered
2	9 mo/M	NICU	Abdominal and cardiac surgery, CVC, ventilator, prolonged stay, ICU admission	CLABSI	Yes <i>Serratia</i> spp	Meropenem + vancomycin	Meropenem	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	Meropenem + vancomycin	Died after 8 days
6	2 y/F	PICU	Congenital central hypoventilation 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	Septic shock	Yes <i>Serratia</i> 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, ESRD, 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, CVA	No	Meropenem	Meropenem	Recovered
12	46 y/M	Nephrology ward	CKD, CVC, prolonged ABX use, prolonged stay	CLABSI	No	Vancomycin	Ciprofloxacin	Recovered

DM, diabetes mellitus; ABX, antibiotic; HTN, hypertension; HF, heart failure; CHF, congestive heart failure; CKD, chronic kidney disease; ESRD, 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.

TABLE 2. Result of antimicrobial susceptibility testing

Antibiotic	Case number											
	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
Gentamycin	R	R	R	R	R	R	R	R	R	R	R	R
Ceftazidime	R	R	R	R	R	R	R	R	R	R	S	R
Ciprofloxacin	R	R	S	S	R	S	S	S	S	R	R	S
Ceftriaxone	R	R	R	R	R	R	R	R	R	R	R	R
Imipenem	R	R	R	R	R	R	R	R	R	R	R	R
Levofloxacin	S	S	S	S	S	S	S	S	S	S	R	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	S	R	R	R	R
Tetracycline	R	R	R	R	R	R	R	R	R	R	S	S
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  $\beta$ -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  $\beta$ -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  $\beta$ -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.

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