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Research Article

CLINICAL FEATURES AND ANTIMICROBIAL SUSCEPTIBILITIES OF *ELIZABETHKINGIA MENINGOSEPTICA* - AN EMERGING PATHOGEN FROM A TERTIARY CARE HOSPITAL IN MANGALORE

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ABSTRACT

Objectives: *Elizabethkingia meningoseptica* has been known to infect the immunocompromised, preterm children, those exposed to antibiotics in critical care units, and those with comorbidities. Multidrug resistance seen in *E. meningoseptica* makes it daunting to choose the right antimicrobial agents for treating infections caused by this organism. The present study was undertaken to establish the incidence of *E. meningoseptica* infections, to investigate the clinical features and risk factors associated with these infections, and to study the antimicrobial susceptibility pattern of *E. meningoseptica* isolates over 2 years.

Methods: Medical records of the patient positive for *E. meningoseptica* from January 2015 to December 2016 were studied retrospectively. The demographic and clinical data of the patients and the antibiotic sensitivity patterns were collected and analyzed.

Results*: E. meningoseptica* was isolated from 13 patients. The mean age was 71.09 years with males being more frequently infected (81.8%). Maximum isolates were from blood (38.5%) with sepsis being the final diagnosis in 53.8% of the patients, followed by respiratory tract infection (46.1%). Two pediatric patients presented with both sepsis and meningitis. Nine patients (69.2%) recovered, and death occurred in four patients (30.8%). Susceptibility testing revealed 100% *in vitro* resistance to most of the antibiotics such as amikacin, aztreonam, cefepime, ceftazidime, colistin, gentamicin, meropenem, and polymyxin B which are used to treat Gram-negative bacterial infections. The isolates were most susceptible to minocycline and piperacillin.

Conclusion: *E. meningoseptica* is an emerging pathogen and is being isolated more frequently now. An expeditious and prompt institution of appropriate therapy is essential because of its inherent resistance to many antimicrobial agents commonly used to treat infections caused by Gram-negative bacteria.

Keywords: Comorbidities, *Elizabethkingia meningoseptica,* Immunocompromised, Multidrug resistance, Hospital.

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INTRODUCTION

Elizabethkingia meningoseptica is a Gram-negative, ubiquitous, non-fermenting, fastidious, obligate aerobic bacillus [1,2]. It has been recognized as a threat to patients in critical care areas because of its multidrug-resistant phenotype and its capability to adapt to various biospheres. It is distributed widely in the hospitals and has been isolated in the hospital environment in water supplies, disinfectants, and medical devices. The virulence of this organism includes the propensity to form biofilms, intracellular invasion, and the ability to survive for long periods in moist environments [3-7].

The incidence of *E. meningoseptica* infections has been increasing over the past decade. Patients at high risk of *E. meningoseptica* infection include preterm children, the immune-compromised, those exposed to antibiotics in critical care units, the presence of underlying diseases, use of central venous catheters, and other invasive medical devices [8,9]. *E. meningoseptica* exhibits chromosomal and plasmid-mediated resistance to many antimicrobial agents which are used to treat Gram-negative bacterial infections such as aminoglycosides and extended-spectrum beta-lactam antibiotics but is susceptible to some agents such as cotrimoxazole, fluoroquinolones, and vancomycin which are used for Gram-positive bacteria [10-12]. Choosing the right antimicrobial agents for patients with *E. meningoseptica* infections is difficult because of the lack of interpretive minimum inhibitory concentration of antibiotics for *E. meningoseptica*, the lack of analysis of clinical response, and choices of antimicrobial agents in the literature [11,13]. Patients with *E. meningoseptica* bacteremia have the poor prognosis, and the use of inappropriate antibiotics can further complicate the situation. Hence, it is essential for proper antimicrobial susceptibility testing before choosing the antimicrobial agents.

In the past decade, we have observed that the number of patients with *E. meningoseptica* infections is increasing. This study retrospectively reviewed the epidemiology, risk factors, clinical features, and antimicrobial resistance patterns associated with this *E. meningoseptica* infections in our geographical area over 2 years period. Furthermore, the antimicrobial susceptibility pattern of the isolates was also analyzed.

METHODS

This study was a retrospective study conducted in an 850-bed referral hospital in Mangalore after approval from the institutional ethics committee. All clinical samples positive for *E. meningoseptica* from January 2015 to December 2016 were included in this study. The details of the patients were obtained from the Medical Records Department. Demographic and clinical data including age, gender, and clinical manifestations were noted. Besides, information on underlying diseases and other associated symptoms during the episode, type of infection, use of invasive procedures, duration of intensive care unit stay, and the outcomes was obtained and analyzed.

Identification and antimicrobial sensitivity testing for the blood culture isolates were done in the Vitek 2 automated system. Antimicrobial sensitivity testing for isolates from other specimens was done by Kirby–Bauer disc diffusion method. The interpretation of antibiotic sensitivity tests was done according to standards for the non-*Enterobacteriaceae,* set by the Clinical and Laboratory Standards Institute.

RESULTS AND DISCUSSION

In this retrospective study of 2 years' duration from January 2015 to December 2016, *E. meningoseptica* was isolated from 13 patients. The bacteria were isolated in four patients from January 2015 to December 2015 and in nine patients from January 2016 to December 2016. Among 13 patients, 11 were adults and 2 were neonates. The average age of the patients was 71.09 years (excluding the two neonates), varying from 42 to 92 years. The adult patients included nine males (81.8%) and two females (18.2%).

All the adult patients had underlying diseases, including diabetes mellitus (DM) (n=6, 54.5%), chronic obstructive pulmonary disease (COPD) (n=4, 36.4%), and malignancy (n=3, 22.3%), chronic urinary system illness (n=4, 36.4%) which included hydroureteronephrosis, renal failure, and urinary tract infection (UTI). Both the neonates were male and had no underlying diseases nor were they premature (Table 1).

All isolates were obtained from hospitalized patients. Maximum number of isolates were from blood (n=5, 38.5%), followed by suction tip (n=3, 23.1%), bronchoalveolar lavage (BAL) (n=2, 15.4%), and cerebrospinal fluid (CSF) (n=2, 15.4%) (Table 1).

Sepsis was the final diagnosis in seven patients (53.8%), whereas six patients (46.1%) had lower respiratory tract infection, two patients (15.4%) had meningitis, and one patient (7.7%) had wound infection. The two pediatric patients presented with both sepsis and meningitis. Nine patients (69.2%) recovered from their infective status, whereas death occurred among four patients (30.8%). The average duration spent in the Intensive Care Unit was found to be 32 days (6–132 days) (Table 1).

All the adult patients were on broad-spectrum antimicrobial regimens before acquiring the infection.

Six patients (46.2%) had concomitant pathogens isolated along with *E. meningoseptica*. The susceptibility testing revealed *in vitro* resistance to most of the antibiotics used to treat Gram-negative bacteria. The susceptibilities of the *E. meningoseptica* isolates to piperacillin/tazobactam, cotrimoxazole, and levofloxacin were found to be 60%, 53.3%, and 38.5%, respectively. The most effective drugs were minocycline and piperacillin with 100% susceptibility (Fig. 1)

DISCUSSION

Recent reports indicate an increase in the incidence of infections by *E. meningoseptica* [11]. In our study, although the number of infections detected was less, a higher rate was observed in the other half of the study period as explained by the increase in the number of cases from 4 in 2015 to 9 in 2016. The above data indicate that there has been a rise in the incidence of infections caused by *E. meningoseptica.*

E. meningoseptica was isolated from 13 patients, 11 were adults, and 2 were neonates. The mean age of the patients was 71.09 years (excluding the two neonates), with a strong preference for extremes of the period with 81.8% being male patients. In a study conducted in Central Taiwan, the mean age of the patient was 72.2 years (excluding one child patient), of which 79.9% were male [14].

In our study, all the adult patients had significant underlying diseases, the most frequent being DM (54.5%), followed by COPD (36.4%), malignancy (22.3%), and chronic urinary tract illness (22.3%). Earlier studies have also reported nosocomial infections by *E. meningoseptica*, predominantly in patients with severe underlying diseases, prolonged hospitalization, treatment with invasive procedures, prior use of broad-spectrum antimicrobials, and associated infections. In a study conducted in a Medical Center in Taiwan, the most common underlying disease was malignancy (35.6%) followed by DM (25.4%) [11]. The possible explanation for our patients to have a higher rate of DM as an underlying disease could be because of the higher prevalence of this condition in India [15]. *E. meningoseptica* has been reported to cause sepsis, meningitis, and pneumonia among neonates, especially

Table 1: Clinical profile of 13 patients with *E. meningoseptica* infections

Year	Age/Sex	Infection	Underlying disease	Source	WBC count/ml	ICU stay (days)	Outcome
2016	66 years/Male	Sepsis	DM, HTN, BA	Blood	14,700	6	Improved
2016	60 years/Male	LRTI	DM, HTN, COPD, Aspergilloma, HUN	Sputum	11,500	51	Improved
2016	65 years/Male	LRTI	Carcinoma lung, Addison's disease, Frontal lobe contusion	Aspirate from lung	14,600	11	Improved
2016	42 years/Male	Sepsis	Multiorgan failure, IHD, Pancreatic pseudocyst	Blood	20,100	10	Expired
2016	75 years/Male	LRTI	DM, HTN, chronic renal failure, LV dysfunction	ET suction tip	20,100	16	Expired
2016	92 years/Male	Sepsis, wound infection	DM, HTN, Carcinoma colon, COPD	Swab	20,600	42	Expired
2016	83 years/Female	LRTI	DM, HTN, BA, CCF, IHD, GB syndrome, UTI, aspiration pneumonia	Tracheostomy suction tip	10,600	61	Expired
2016	3 days/Male	Sepsis, meningitis	none	Blood, CSF	18,200	14	Improved
2016	17 days/Male	Sepsis, meningitis	none	Blood, CSF	16,400	28	Improved
2016	73 years/Male	LRTI	COPD, PTB, bronchiectasis	BAL	20,000	12	Improved
2016	79 years/Male	Sepsis	Subdural hemorrhage	Catheter tip	20,900	132	Improved
2015	70 years/Male	Sepsis	DM, COPD, Ca. colon, renal failure	ET catheter tip	7,800	17	Improved
2015	77 years/Female	LRTI	HTN, IHD, PTB, pneumonia	BAL	17,000	19	Improved

DM: Diabetes mellitus, HTN: Hypertension, COPD: Chronic obstructive pulmonary disease, BA: Bronchial asthma, HUN: Hydroureteronephrosis, IHD: Ischemic heart disease, CCF: Congestive cardiac failure, GB syndrome: Guillain–Barre syndrome, UTI: Urinary tract infection, PTB: Pulmonary tuberculosis, BAL: Bronchoalveolar lavage, CSF: Cerebrospinal fluid, ET-Endotracheal. *E. meningoseptica: Elizabethkingia meningoseptica*

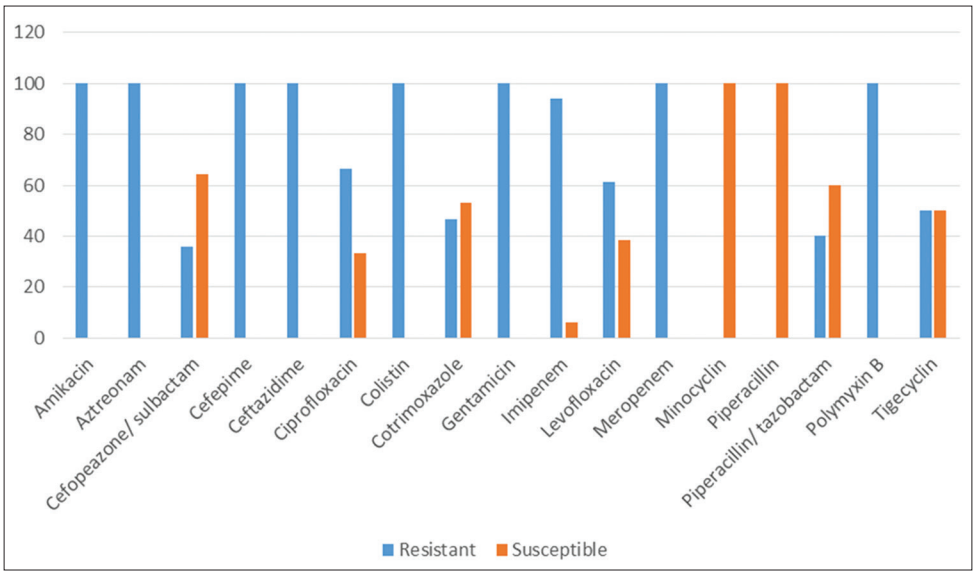

Fig. 1: Antibiotic susceptibility pattern of *Elizabethkingia meningoseptica*

premature infants [1,16]. In our study, *E. meningoseptica* was isolated from two neonates, both males with sepsis and meningitis. However, the neonates had no underlying disease nor were they premature.

The predominant source for culture in our study for most of the *E. meningoseptica* isolates was from blood (38.5%), followed by suction tip (23.1%), BAL (15.4%), and CSF (15.4%). In a study conducted by Chang *et al*., the primary source was blood (48.7%) followed by sputum (41%) [14]. Another study conducted in a Trauma Center in New Delhi showed that the primary source for culture was BAL (70%), followed by blood (22%) and CSF (4%) [17]. Various studies have described *E. meningoseptica* as an etiological agent of meningitis, sepsis, pneumonia, endocarditis, bacteremia, cellulitis, wound infection, endophthalmitis, keratitis, and UTI [1,18-21]. In our study, sepsis was found to be the diagnosis in 53.8% of patients, followed by lower respiratory tract infection (46.1%), meningitis (15.4%), and wound infection (7.7%). All the adult patients in our study were on broad-spectrum antibiotics such as meropenem and third-generation cephalosporins before acquiring the infection. This observation is comparable to the results obtained in a survey conducted by Rastogi *et al*., wherein all the patients too were on broad-spectrum antibiotics before procuring the infection [17]. Thus, we can consider that the increased use of broad-spectrum antibiotics against other multidrug-resistant Gram-negative organisms such as *Acinetobacter* spp. and *Klebsiella pneumoniae* could lead to superinfection with *E. meningoseptica* [22].

Several studies have confirmed *E. meningoseptica* to be a common contaminant of various medical devices such as mechanical ventilators, intubation tubes, syringes, intravenous catheters, and prosthetic valves [6,23-25]. In our study, these bacteria were isolated from patients who were on mechanical ventilators (25.9%), intravenous catheters (22.2%), intubation tubes (24.8%), and bronchoscopy endotracheal tubes (11.1%). The infections due to these bacteria in our study cannot be attributed to contaminated devices only as no attempt was made to isolate the organism from the medical devices. Precautionary measures should be used in the treatment of patients on mechanical ventilators and those who are transferred to acute care hospitals with infections caused by this organism as suggested by Weaver *et al.* [26].

Infections with *E. meningoseptica* were associated with poor outcome, with mortality varying from 23% to 52% as given by several studies [11]. The risk factors for the poor outcome could be the presence of central venous line infection, inappropriate use of antibiotics, prolonged hospital stay, and the possible presence of a high biofilm-forming organism [3]. The 28-day mortality in a study conducted by Lin *et al*. was found to be 41% [13]. In our study, the mortality was 30.8% with the patients predominantly suffering from sepsis and lower respiratory tract infections, with only 69.2% of the patients recovering from their infective status. All the patients in our study had prolonged hospital stay with a range from 6 to 132 days (mean=32 days). Our findings are similar to the result of Lin *et al*. where the mean duration of hospital stay was 32 days (range 13–99 days) [18]. However, in a study conducted during an outbreak of *E. meningoseptica* in London, the mean duration of hospital stay was found to be 17 days (range 4–35 days) [27]. Six patients (46.2%) in our study had concomitant pathogens such as *Pseudomonas aeruginosa, K. pneumoniae, Acinetobacter baumannii, Proteus mirabilis, Sphingomonas paucimobilis, Stenotrophomonas maltophilia,* and methicillin-resistant *Staphylococcus aureus*. The isolation of concomitant pathogens makes it difficult to explain the pathogenic role of *E. meningoseptica.*

The antibiotic sensitivity pattern of *E. meningoseptica* varies across the reported literature. The organism was said to be resistant to most of the β-lactam antibiotics including carbapenems and aztreonam, the aminoglycoside group of drugs and chloramphenicol, but was susceptible to drugs such as cotrimoxazole, fluoroquinolones, minocycline, tigecycline, and piperacillin [7,9,11,12,14,25]. Studies investigating the resistance of *E. meningoseptica* have discovered this unusual antimicrobial sensitivity pattern to be due to its production of metallo-β-lactamases coded by BlaB and Bla (GOB) genes, conferring the ability to degrade most of the β-lactam antibiotics, thereby restraining their usefulness as a therapeutic option [10]. This high-level antibiotic resistance may be the reason for the appearance of this organism in our patients who were all on broad-spectrum antibiotics. The antibiotic susceptibility testing by Kirby–Bauer disc diffusion method revealed resistance to amikacin (100%), gentamicin (100%), aztreonam (100%), cefepime (100%), ceftazidime (100%), meropenem (100%), imipenem (93.8%), polymyxin B (100%), colistin (100%), and tigecycline (50%). The susceptibilities of our isolates to piperacillin/tazobactam, cotrimoxazole, and levofloxacin were found to be 60%, 53.3%, and 38.5%, respectively. The most effective drugs were minocycline and piperacillin with 100% susceptibility. Previous reports have also demonstrated 100% susceptibility of the bacteria toward minocycline [1,14].

To conclude, *E. meningoseptica* is an emerging pathogen and is being isolated more frequently now, especially in patients with severe underlying diseases, prolonged hospitalization, treatment with invasive procedures, and prior use of broad-spectrum antimicrobials. Rapid diagnosis and timely institution of appropriate therapy are essential

because of its inherent resistance to many antimicrobial agents commonly used to treat infections caused by Gram-negative bacteria.

CONCLUSION

E. meningoseptica was isolated from 13 patients. The mean age was 71.09 years with males being more frequently infected (81.8%). Maximum isolates were from blood (38.5%) with sepsis being the final diagnosis in 53.8% of the patients, followed by respiratory tract infection (46.1%). Two pediatric patients presented with both sepsis and meningitis. Nine patients (69.2%) recovered, and death occurred in 4 patients (30.8%). Susceptibility testing revealed 100% *in vitro* resistance to most of the antibiotics such as amikacin, aztreonam, cefepime, ceftazidime, colistin, gentamicin, meropenem, and polymyxin B which are used to treat Gram-negative bacterial infections. The isolates were most susceptible to minocycline and piperacillin. *E. meningoseptica* is an emerging pathogen and is being isolated more frequently now. An expeditious and prompt institution of appropriate therapy is essential because of its inherent resistance to many antimicrobial agents commonly used to treat infections caused by Gram-negative bacteria.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

REFERENCES

1. Bloch KC, Nadarajah R, Jacobs R. *Chryseobacterium meningosepticum:* An emerging pathogen among immunocompromised adults. Medicine (Baltimore) 1997;76:30-41.
2. Henriques IS, Araújo S, Azevedo JS, Alves MS, Chouchani C, Pereira A, *et al*. Prevalence and diversity of carbapenem-resistant bacteria in untreated drinking water in Portugal. Microb Drug Resist 2012;18:531-7.
3. 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.
4. Jiang X, Wang D, Wang Y, Yan H, Shi L, Zhou L. Occurrence of antimicrobial resistance genes sul and dfrA12 in hospital environmental isolates of *Elizabethkingia meningoseptica*. World J Microbiol Biotechnol 2012;28:3097-102.
5. Ceyhan M, Yildirim I, Tekeli A, Yurdakok M, Us E, Altun B. A *Chryseobacterium meningosepticum* outbreak observed in 3 clusters involving both neonatal and non-neonatal pediatric patients. Am J Infect Control 2008;36:453-7.
6. Hoque SN, Graham J, Kaufmann ME, Tabaqchali S. *Chryseobacterium (Flavobacterium) meningosepticum* outbreak associated with colonization of water taps in a neonatal intensive care unit. J Hosp Infect 2001;47:188-92.
7. Ghafur A, Vidyalakshmi PR, Priyadarshini K, Easow JM, Raj R, Raja T. *Elizabethkingia meningoseptica* bacteremia in immunocompromised hosts: The first case series from India. South Asian J Cancer 2013;2:211-5.
8. Tak V, Mathur P, Varghese P, Misra MC. *Elizabethkingia meningoseptica*: An emerging pathogen causing meningitis in a hospitalized adult trauma patient. Indian J Med Microbiol 2013;31:293-5.
9. Ratnamani MS, Rao R. *Elizabethkingia meningoseptica:* Emerging nosocomial pathogen in bedside hemodialysis patients. Indian J Crit Care Med 2013;17:304-7.
10. Gonzalez LJ, Vila AJ. Carbapenem resistance in *Elizabethkingia meningoseptica* is mediated by metallo-β-lactamase BlaB. Antimicrob Agents Chemother 2012;4:1686-92.
11. 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 centre in Taiwan, 1999–2006. Eur J ClinMicrobiol Infect Dis 2011;30:1971-8.
12. Pereira GH, Garcia DO, Abboud CS, Barbosa VL, Silva PS. Nosocomial infections caused by *Elizabethkingia meningoseptica*: An emergent pathogen. Braz J Infect Dis 2013;17:606-9.
13. Lin YT, Chiu CH, Chan YJ, Lin ML, Yu KW, Wang FD. Clinical and microbiological analysis of *Elizabethkingia meningoseptica* bacteremia in adult patients in Taiwan. Scand J Infect Dis 2009;41:628-34.
14. Chang YC, Lo HH, Hsieh HY, Chang SM. Identification and epidemiological relatedness of clinical *Elizabethkingia meningoseptica* isolates from central Taiwan. J Microbiol Immunol Infect 2014;47:318-23.
15. Kaveeshwar SA, Cornwall J. The current state of diabetes mellitus in India. Australas Med J 2014;7:45-8.
16. Ceyhan M, Celik M. Elizabethkingia meningosepticum (*Chryseobacterium meningosepticum*) infections in children. Int J Pediatr 2011;2011:215237.
17. Rastogi N, Mathur P, Bindra A, Goyal K, Sokhal N, Kumar S, *et al*. Infections due to *Elizabethkingia meningoseptica* in critically injures trauma patients: A seven-year study. J Hosp Infect 2016;92:30-2.
18. Lin PY, Chu C, Su LH, Huang CT, Chang WY, Chiu CH. Clinical and microbiological analysis of bloodstream infections caused by *Chryseobacterium meningosepticum* in nonneonatal patients. J Clin Microbiol 2004;7:3353-5.
19. Connell PP, Wickremasinghe S, Devi U, Waters MJ, Allen PJ. Self-induced *Elizabethkingia meningoseptica* endophthalmitis: A case report. J Med Case Rep 2011;5:303.
20. Hagiya H, Ogawa H, Takahashi Y, Hasegawa K, Iwamuro M, Otsuka F. A nephrostomy-associated urinary tract infection caused by *Elizabethkingia meningoseptica*. Intern Med 2015;54:3233-6.
21. Yang YS, Chun JW, Koh JW. Keratitis with *Elizabethkingia meningoseptica* occurring after contact lens wear: A case report. Korean J Ophthalmol 2013;27:133-6.
22. Jung SH, Lee B, Mirrakhimov AE, Hussain N. Septic shock caused by *Elizabethkingia meningoseptica:* A case report and review of the literature. BMJ Case Rep 2013;2013. pii: bcr2013009066.
23. du Moulin GC. Airway colonization by *Flavobacterium* in an intensive care unit. J Clin Microbiol 1979;10:155-60.
24. Nulens E, Bussels B, Bols A, Gordts B, Van Landuyt HW. Recurrent bacteremia by *Chryseobacterium indologenes* in an oncology patient with a totally implanted intravascular device. Clin Microbiol Infect 2001;7:91-3.
25. Maraki S, Scoulica E, Manoura A, Papageorgiou N, Giannakopoulou C, Galanakis E. A *Chryseobacterium meningosepticum* colonization outbreak in a neonatal intensive care unit. Eur J Clin Microbiol Infect Dis 2009;28:1415-9.
26. Weaver KN, Jones RC, Albright R, Thomas Y, Zambrano CH, Costello M, *et al*. Acute emergence of *Elizabethkingia meningoseptica* infection among mechanically ventilated patients in a long-term acute care facility. Infect Control Hosp Epidemiol 2010;31:54-8.
27. Moore LS, Owens DS, Jepson A, Turton JF, Ashworth S, Donaldson H, *et al.* Waterborne *Elizabethkingia meningoseptica* in adult critical care. Emerg Infect Dis 2016;22:9-17.