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LETTER TO THE EDITOR

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Bacteremia caused by *Elizabethkingia meningoseptica* in a mechanically ventilated patient successfully treated with imipenem-cilastatin and ciprofloxacin

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Dear editor

Elizabethkingia meningoseptica is ubiquitous in soil and water as well as in hospital environments[1,2,3]. Thus, nosocomial outbreaks of *E. meningoseptica* can result from exposure to contaminated water sources or medical devices[2]. Due to the therapeutic challenge resulting from multi-drug resistance, recognition and treatment of *E. meningoseptica* is of paramount importance for clinicians[2,3]. We report a case of bacteremia due to a multi-drug resistant *E. meningoseptica* in a patient who required assisted ventilation due to respiratory failure.

A 62-year-old male, who had had a history of oral cancer with operation and concurrent chemoradiotherapy, diabetes mellitus, bilateral vocal palsy, upper airway obstruction followed by tracheostomy and chronic obstructive pulmonary disease, developed cough with shortness of breath prior to admission. He was admitted to the intensive care ward because of impending respiratory failure. Ventilation support with Evita 4 (Dräger, Lubeck, Germany) was used, and he was transferred to the respiratory care center (RCC) for weaning twenty-one days later, because of fluctuations in his respiratory condition associated with underlying pulmonary problems. A new fever episode appeared on the 11th day after transfer to RCC (Figure 1). The lungs showed crackles on the right side. Laboratory analyses revealed a white blood cell count of 10,800 cells/ mm^3. The serum creatinine level was 2.3 mg/dL. The chest X-ray showed a new pneumonic patch over the left lower lobe. *E. meningoseptica* (2/2 sets) was identified by using matrix-assisted laser desorption ionization-time of flight mass spectrometry (bioMerieux, Hazlewood, Mo.). An antimicrobial drug susceptibility test[4] was conducted for *E. meningoseptica* by using the bioMérieux VITEK 2 system (bioMerieux, Hazlewood, MO.), and the minimum inhibitory concentration (MIC) was measured for each of the following antimicrobial drugs: piperacillin-tazobactam, cefotaxime, flomoxef, ceftazidime, cefepime, cefoperazone, amikacin, gentamicin, ciprofloxacin, levofloxacin, imipenem-cilastatin, meropenem, trimethoprim-sulfamethoxazole, doxycycline and colistin (Table 1). In addition, MIC results determined by the Epsilometer test (AB Biodisk, Sweden system) were: ciprofloxacin ≧4 μg/mL; levofloxacin ≧8 μg/mL; imipenem-cilastatin ≧16 μg/mL; meropenem ≧16 μg/mL; trimethoprim-sulfamethoxazole ≧4/ 76 μg/mL; and vancomycin ≧16 μg/mL. The patient received a combination of intravenous ciprofloxacin (200 mg every 12 hours) and imipenem-cilastatin (250 mg every 6 hours). His condition stabilized gradually and the follow-up chest X-ray showed improvement. Due to difficulty in weaning, he was transferred to a respiratory care ward after 42 days of hospitalization at RCC. No outbreak of *E. meningoseptica* infection was reported during the period of hospitalization at RCC. The follow-up of microbiological analyses for this patient did not show *E. meningoseptica* infection.

The appropriate choice of antibiotics for treatment of *E. meningoseptica* infection is difficult because optimal antimicrobial guidelines remain to be established[2,3]. Herein, the antimicrobial drug susceptibility test of this *E. meningoseptica* showed resistance to all the antibiotics, including trimethoprim-sulfamethoxazole

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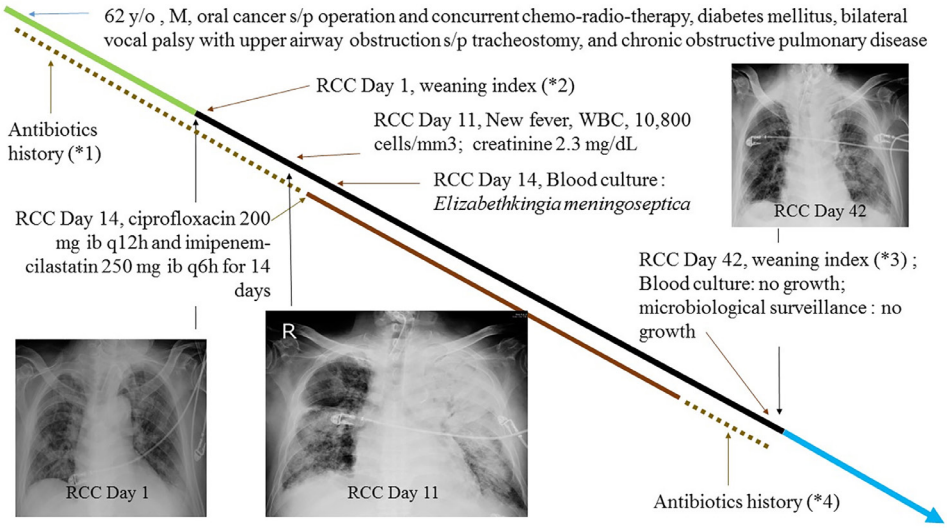

Figure 1 - Timeline of the *Elizabethkingia meningoseptica* infection, serial chest X-ray images and serial antibiotics history
Green Line: medical intensive care unit; **Black Line:** respiratory care center; **Blue Line:** respiratory care ward; **Brown Line:** antibiotics regimen for *Elizabethkingia meningoseptica*; **Brown dot line:** history of antibiotics usage.
Notes: [1]Antibiotics history: flomoxef 1,000 mg ib q12h (MICU Day1 - MICU Day 6) for empirical therapy; ciprofloxacin 200 ib q12h (MICU Day 6-MICU Day 8) for coverage of *P. aeruginosa*, and stop ciprofloxacin due to no significant evidence of pulmonary infection by *P. aeruginosa*; no antibiotics (MICU Day 8- RCC Day 11); piperacilin 3,000 mg ib q6h (RCC Day 11- RCC Day 14) empirically for new fever episode. [2]weaning index: synchronized intermittent mode was 6/minute with pressure support 16 cmH_2O, FiO_2 was 30 %, positive end-expiratory pressure was 5 cmH_2O, rapid shallow breathing index was 96. [3]weaning index: bi-level positive airway pressure mode assisted with pressure control mode 22/ minute, FiO_2 was 30%, positive end-expiratory pressure was 8 cmH_2O, tidal volume was 455 cm H_2o, ventilation rate was 16/ minute, total mechanical volume was 10.9 L /minute. [4]Antibiotics history: No prescription of antibiotics (RCC Day 28- RCC Day 42).
Abbreviation: ib: in bag drip; M, male; MICU: medical intensive care unit; RCC: respiratory care center; s/p, status of post; WBC: white cell count.

Table 1 - Susceptibilities of this isolate to the antimicrobial agents

	E-test [3]	VITEK 2[4]	MIC interpretation criteria (μg/mL)		
Antimicrobial agent [1]	This isolate		S	I	R
Amikacin		≧64	≤ 16	32	≥ 64
Cefepime		≧32	≤ 8	16	≥ 32
Cefoperazone		≧64	≤ 16	32	≥ 64
Cefotaxime		≧32	≤ 8	16-32	≥ 32
Flomoxef		≧64	(pending)		
Ceftazidime		≧32	≤ 8	16	≥ 32
Ciprofloxacin	≧4	≧4	≤ 1	2	≥ 4
Colistin		≧16	≤ 2	4	≥ 8
Doxycycline		≧16	≤ 4	8	≥ 16
Gentamicin		≧16	≤ 4	8	≥ 16
Imipenem	≧16	≧16	≤ 4	8	≥ 16
Levofloxacin	≧8	≧8	≤ 2	4	≥ 8
Meropenem		≧16	≤ 4	8	≥ 16
Minocycline		≧16	≤ 4	8	≥ 16
Piperacillin/tazobactam		≧128	≤ 16/4	32/4-64/4	≥ 32/4
Trimethoprim/sulfamethoxazole	≧4/76	≧4/76	≤ 2/38	-	≥ 4/76
Vancomycin[2]	≥ 16		≤ 2	4-8	≥ 16

Notes: [1]The Clinical and Laboratory Standards Institute (CLSI) minimum inhibitory concentration (MIC) breakpoints for non-Enterobacteriaceae were applied for all antimicrobial agents except for vancomycin and flomoxef [Clinical and Laboratory Standards Institute. 2016. M100-S26: performance standards for antimicrobial susceptibility testing, 26th informational supplement. CLSI, Wayne, PA.]. [2]The CLSI MIC breakpoint for Staphylococcus spp. was applied to vancomycin. [3]Antimicrobial drug susceptibility test was conducted by using the Epsilometer test (AB Biodisk, Sweden system). [4]Antimicrobial drug susceptibility test was conducted by using the bioMérieux VITEK 2 system (bioMerieux, Hazlewood, MO.). Abbreviation: CLSI: Clinical and Laboratory Standards Institute; I: intermediate; MIC: minimal inhibitory concentration; S: susceptible; R: resistant.

and vancomycin[5]. However, the bacteremia caused by *E. meningoseptica* was successfully treated in this case with a two-week administration of imipenem-cilastatin and ciprofloxacin. In terms of generalization, this case description is limited by the restricted number of clinical studies in the literature[2,3], the lack of minimum inhibitory concentration breakpoints of antimicrobial agents to *E. meningoseptica*[4], and the paucity of 16S rRNA sequencing data due to the inability to perform a reliable 16S rRNA sequencing analysis without a valid positive control[6].

We suggest a combination therapy as an alternative for treatment of multi-drug resistant *E. meningoseptica* infection and undertaking active surveillance of *E. meningoseptica* infections because *E. meningoseptica* outbreaks could subsequently result from exposure to contaminated water sources or medical devices.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

ETHICS STATEMENTS

This study was approved by the Changhua Christian Hospital (CCH) Institutional Review Board (CCH IRB Nº 131221) for human subjects

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AUTHORS CONTRIBUTION

CHC conceived and designed this study. CHC analyzed the data, wrote the paper, prepared figures and tables. CHC, CHL and JSL assisted the patient. CHC handled the literature review. JSL performed the experiments. All authors reviewed the drafts of the paper.

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