Epidemiological Study and Analysis of Risk Factors for Elizabethkingia Meningoseptica Infection in a Large General Hospital in China

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Research

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Abstract

Background

As a kind of nosocomial infection pathogen which can cause high mortality, its susceptibility and death risk factors are still unclear.

Aim

To analyze the epidemiological characteristics of and risk factors for *Elizabethkingia meningoseptica* infection.

Methods

Relevant literature from 2011 to 2019 with the key words "*E. meningoseptica*" or "*Elizabethkingia meningoseptica*" in the title and abstract was retrieved from the PubMed database. The risk factors of infection and death for infected patients treated at Southwest Hospital during the above period were analyzed by logistic regression.

Results

From 2011 to 2019, 366 patients infected with *E. meningoseptica* were reported in 132 articles in the PubMed database. The mortality rate was 63.20%. During the same period, 92 infected patients were treated at our hospital. The overall mortality rate was approximately 28.3% (26/92) to 39.1% (36/92). The resistance rate for carbapenems was 100%; for cephalosporins, it was more than 90%; and for minocycline, it was 0. Central venous catheterization (p < 0.001), mechanical ventilation (p = 0.015), bacteria type (p < 0.001), operation type (p = 0.001), fungal infection (p < 0.001), carbapenem use (p = 0.000), and triazole use (p = 0.016) were independent risk factors for *E. meningoseptica* infection. According to logistic regression, bacteria type (p = 0.037), platelet level (p = 0.014), and mechanical ventilation (p = 0.043) were risk factors for death.

Conclusion

The incidence of *E. meningoseptica* infection worldwide shows a trend toward increasing yearly. Invasive operations, multiple bacterial or fungal infections and the use of carbapenems may be predisposing factors, and platelet level, bacteria type, and mechanical ventilation were risk factors for death.

1 Introduction

*Elizabethkingia meningoseptica* is a nonfermenting gram-negative bacterium that can produce light yellow pigments, is motility negative and oxidase positive, and is widely distributed in water, soil, and hospital tap water but rarely infects humans[1]. Since the first report human infection caused by *E. meningoseptica* in 1959, an increasing number of countries and regions have reported infections with this pathogen in humans, livestock, poultry, and other animals, and the bacterium has gradually become a leading pathogen that endangers the lives of patients [2]. Between November 1, 2015, and March 30, 2016, Wisconsin (56 cases) and Michigan (1 case) reported 57 cases, including 18 deaths. Most of these patients infected with *E. meningoseptica* were elderly people over 65 years old with serious comorbidities. Patients with diabetes, malignant tumors, hypertension, and other comorbidities; those with compromised immunity; and those undergoing immunosuppressive treatment are more likely than other groups to be infected with *E. meningoseptica.*
Infection can manifest as meningitis, bacteremia, pneumonia, and skin and soft tissue infections, and the mortality rate can reach 63.20%[3]. Inappropriate empirical antimicrobial therapy has been shown to be an independent risk factor for death in patients infected with *E. meningoseptica* [4]. So, understanding the risks of *E. meningoseptica* infection maybe helpful to treat these patients in future.

2 Materials And Methods

The First Affiliated Hospital of the Third Military Medical University is a large, comprehensive, first-class tertiary hospital in Western China. To understand the epidemiological characteristics of *E. meningoseptica* on a global scale and in Chinese hospitals and to understand the risk factors for related infection and death, we reviewed relevant papers in the PubMed database from 2011 to 2019 and retrospectively analyzed the data of patients infected by *E. meningoseptica* at our hospital during the same period, with the aim of providing a reference for the clinical prevention and treatment of *E. meningoseptica* infection. This study was approved by the Ethics Committee of The First Affiliated Hospital of the Third Military Medical University (Army Medical University), China.

2.1 Global epidemiological study of *E. meningoseptica* infection

As of December 31, 2019, we searched PubMed using “*E. meningoseptica*” as the keyword to identify articles containing “*E. meningoseptica*” in the title and abstract during the period 2011–2019, and we analyzed the type and number of literature reports and the regions from which they derived in different years. We reviewed individual epidemiological articles related to *E. meningoseptica* infection in different regions over the 9-year period to understand the important epidemiological characteristics of patients with *E. meningoseptica* infection, such as sex, age, number of cases, and fatality rate.

2.2 Data collection for hospitalized patients

The age, sex, disease type, department distribution, and disease severity of patients hospitalized at our hospital from January 1, 2011, to December 31, 2019 who were found to have *E. meningoseptica* infection were collected. Patients who were treated at the same department during the same period were randomly matched into this study at a 1:2 ratio according to the above five factors. The data of general characteristics sex, age, disease severity, body mass index (BMI) department distribution, central venous catheterization (CVC), mechanical ventilation, bacteria type, operation, fungal infection, antimicrobial use, white blood cell count (N), platelet (PLT) count and Neutrophil ratio (N%) for all of the above patients were collected.

2.3 Collection of data regarding risk factors for death

We collected data regarding BMI, bacteria type, disease severity, age, sex, operation type, need for mechanical ventilation, CVC, fungal infection, and other indicators for patients who died and those who survived after infection with *E. meningoseptica*. Ten of these patients ceased treatment at our hospital for personal reasons, and we were unable to determine their death or survival.

2.4 Bacterial isolates

All clinical specimens were inoculated according to the standards of the Clinical and Laboratory Standards Institute (CLSI) and incubated overnight in an incubator at 35 ± 2°C. A VITEK-2 compact was used for the routine identification of strains, and strains were randomly selected for further confirmation of bacterial species using a matrix-assisted laser desorption/ionization (MALDI)-time-of-flight (TOF) mass spectrometer. Minimal inhibitory concentration (MIC) was used to detect the susceptibility of these strains to 16 antimicrobials and combinations of antimicrobials: piperacillin, piperacillin/tazobactam, ceftazidime, cefotaxime, cefepime, aztreonam, imipenem, meropenem, amikacin, gentamicin,
netilmicin, tobramycin, ciprofloxacin, levofloxacin, trimethoprim/sulfamethoxazole, and minocycline. *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853 were the quality control strains for determining antimicrobial susceptibilities.

### 2.5 Study design

All the patients were divided into two groups: infected group and non-infected group to find the risks of *E. meningoseptica* infection. Patients who died and those who survived after infection with *E. meningoseptica* were studied to find the risks of death. Here, it needed to be noted that ten of these infected patients discontinued the treatment for personal reasons, and we were unable to determine their death or survival.

### 2.6 Statistical analysis

The number of strains detected and their susceptibilities to antimicrobials were analyzed using Whonet 5.6, and the patients’ general information, risk factors for infection, and risk factors for death were analyzed using logistic regression and *t*-test by SPSS 22.0.

### 3 Results

#### 3.1 Global epidemiological characteristics of *E. meningoseptica*

The PubMed query yielded 132 articles containing *E. meningoseptica* in the title and abstract from the nine years from 2011 to 2019. The literature showed that *E. meningoseptica* was detected in six species (humans, pigs, dogs, birds, insects, and corn) and was reported on five continents (Asia, Europe, America, Africa, and Oceania), of which Asia had the most reports, followed by Europe and America (Table 1). There were 32 epidemiological investigation reports related to *E. meningoseptica* infection, which included 366 infected people; the overall mortality rate of patients with *E. meningoseptica* infection was >20%, and the highest mortality rate was 63.20% (Table 2) [5–18].
Table 1
Literature related to *E. meningoseptica* searched in Pubmed database from 2011 to 2019

| Paper type                          | 2019 | 2018 | 2017 | 2016 | 2015 | 2014 | 2013 | 2012 | 2011 |
|-------------------------------------|------|------|------|------|------|------|------|------|------|
| Diagnostic Techniques               | 3    | 3    | 3    | 1    | 1    | 1    |      |      |      |
| Review                              | 1    | 1    |      |      | 1    | 1    |      |      |      |
| Case report                         | 8    | 4    | 7    | 3    | 5    | 5    | 4    | 1    | 2    |
| Epidemiological Investigation       | 2    | 3    | 1    | 2    | 2    | 1    | 4    | 1    |      |
| Basic research                      | 3    | 1    | 3    | 2    |      | 1    | 2    |      |      |
| Comment                             | 1    | 1    | 3    | 1    |      | 1    |      |      |      |
| Nosocomial Infection                | 1    | 2    | 1    | 1    |      | 2    |      | 1    |      |
| Correction                          |      |      |      |      |      |      |      |      | 1    |
| Genome Announc                      |      |      |      |      |      |      |      |      |      |
| Other                               |      |      |      |      |      |      |      |      |      |
| Other species                       | 1(Pig)| 1(Dog)| 1(Corn)| 1(Bird)| 3(Anopheles, Parasite, Amphibian)| 2(Anopheles, Tilapia mossambica) |
| State                               |      |      |      |      |      |      |      |      |      |
| Asia                                | 14   | 9    | 12   | 6    | 9    | 10   | 9    | 2    | 3    |
| Europe                              | 3    | 4    | 5    | 5    | 4    | 3    | 3    | 1    |      |
| America                             | 4    | 1    | 5    | 5    | 2    | 5    | 2    | 3    |      |
| Africa                              |      |      |      |      |      |      |      |      |      |
| Oceania                             |      |      |      |      |      |      |      |      |      |
| Total                               | 21   | 14   | 22   | 16   | 16   | 14   | 17   | 4    | 8    |
Table 2
Epidemiological literature related to *E. meningoseptica* infection searched in Pubmed database from 2011 to 2019

| Years | NO. | Country  | Cases | Age(years)mean ± SD | Gender | Female no.(%) | Male, no.(%) | mortality rate | references |
|-------|-----|----------|-------|---------------------|--------|--------------|-------------|----------------|------------|
| 2019  | 1   | Singapore| 13    | 0–18(child)         | 8(61.5)| 5(38.5)      | 15.40%      | [5]            |
|       | 2   | Taiwan   | 30    | 74.0 ± 18.2         | 11(36.7)| 19(63.3)     | 46.70%      | [6]            |
| 2018  | 1   | Taiwan   | 20    | 56.6 ± 15.6         | 5(25)  | 15(75)       | 27.20%      | [7]            |
|       | 2   | India    | 4     | 16–54               | 2(50)  | 2(50)        | 3 cases died | [8]            |
| 3     |     | Taiwan   | 19    | 82.0 ± 7.3          | 1(5.3) | 18(94.7)     | 63.20%      | [9]            |
| 2017  | 1   | Taiwan   | 51    | 78.2 ± 12.6         | 26(51) | 25(49)       | 30.7%       | [10]           |
| 2016  | 1   | India    | 21    | 78.2 ± 12.6         | 1(4.8) | 20(95.2)     | 47.60%      | [11]           |
|       | 2   | Hong Kong| 3     | 51–89               | 1(33.3)| 2(66.7)      | 0           | [12]           |
| 2015  | 1   | India,Same as the first in 2016 |     |                     |        |              |             |                |
|       | 2   | China    | 20    | 52(average age)     | 8(40)  | 12(60)       | 10%         | [13]           |
| 2014  | 1   | Taiwan   | 39    | 72.2 ± 14.5         | 8(10.5)| 31(79.5)     | Unaccounted for mortality | [14]          |
| 2013  | 1   | India    | 8     | 3–76                | 4(50)  | 4(50)        | 25%         | [15]           |
|       | 2   | Taiwan,Same as the 2014 |     |                     |        |              |             |                |
|       | 3   | India    | 11    | 48.4(average age)   | 4(36.4)| 7(63.6)      | 17.20%      | [16]           |
|       | 4   | Brazil   | 9     | 0.4–81              | 5(55.5)| 4(44.4)      | 30%         | [17]           |
| 2012  |     | None     |       |                     |        |              |             |                |
| 2011  | 1   | Taiwan   | 118   | 64.12 ± 19          | 48(40.3)| 71(59.7)     | 23.4%       | [18]           |

3.2 General characteristics of patients with *E. meningoseptica* in Southwest Hospital

*E. meningoseptica* was detected in 92 patients at this hospital from 2011 to 2019, including 64 males (69.57%) and 28 females (30.43%). In terms of age distribution, middle-aged patients (aged 40–65 years) accounted for the largest proportion, with 48 cases (52%) in total, followed by elderly patients (aged > 65 years), with 28 cases (30%) (Fig. 1a). Regarding the departmental distribution, the neurosurgery department had the highest detection rate (40.2%), and the surgical and intensive care units (ICUs) had higher detection rates than the general internal medicine department (Table 3). Except for 2011 and 2013, the annual number of infected patients showed an annual increasing trend consistent with the number of papers on *E. meningoseptica* infection published worldwide (Fig. 1b). Of the 92 infected
patients, 26 died (28%) and 56 (61%) survived; for 10 patients (11%), death or survival could not be determined. Therefore, the overall mortality rate of this population was approximately 28.3% (26/92) to 39.1% (36/92) (Fig. 1c).

Table 3
Departmental distribution of 92 patients infected with *E.meningoseptica* in Southwest Hospital from 2011 to 2019

| Department                           | 2019 | 2018 | 2017 | 2016 | 2015 | 2014 | 2013 | 2012 | 2011 | Total |
|--------------------------------------|------|------|------|------|------|------|------|------|------|-------|
| Rehabilitation department            | 1    |      |      |      |      |      |      |      |      | 1(1.0%) |
| Neurosurgery department              | 2    | 19   | 8    | 4    | 1    | 1    | 2    |      |      | 37(40.2%) |
| Intensive care unit                  |      |      |      |      |      |      |      |      |      | 2(2.1%) |
| Department of respiration             | 1    | 1    |      |      |      |      |      |      |      | 2(2.1%) |
| Obstetrical-Gynecology department    |      | 1    |      |      |      |      |      |      |      | 2(2.1%) |
| Joint surgery                        |      | 1    |      |      |      |      |      |      |      | 1(1.0%) |
| Nephrology department                | 1    | 1    |      |      |      |      |      |      |      | 2(2.1%) |
| Intensive care unit                  | 1    | 1    | 1    | 2    | 1    | 2    | 3    | 1    |      | 12(13.0%) |
| General surgery                      | 1    |      |      |      |      |      |      |      |      | 1(1.0%) |
| Department of Cardiovascular Medicine| 1    |      |      |      |      |      |      |      |      | 1(1.0%) |
| Burn department                      | 1    | 1    |      |      |      |      |      |      |      | 2(2.1%) |
| Thoracic surgery                     | 1    |      |      |      |      |      |      |      |      | 1(1.0%) |
| Dermatological department            | 1    |      |      |      |      |      |      |      |      | 1(1.0%) |
| Neurology department                 |      | 2    |      |      |      |      |      |      |      | 2(2.1%) |
| Hepatobiliary surgery                | 1    | 1    | 2    | 4    | 1    |      |      |      |      | 9(9.8%) |
| Oncology department                  |      | 1    |      |      |      |      |      |      |      | 1(1.0%) |
| Pediatrics                           | 1    | 1    |      |      |      |      |      |      |      | 2(2.1%) |
| Emergency department                 | 2    | 1    | 1    | 2    | 1    | 2    |      |      |      | 9(9.8%) |
| Urology department                   |      | 1    |      |      |      |      |      |      |      | 1(1.0%) |
| Geriatrics department                | 1    | 1    |      |      |      |      |      |      |      | 2(2.1%) |
| Ophthalmology department             | 1    |      |      |      |      |      |      |      |      | 1(1.0%) |
| Hematology department                | 1    | 1    |      |      |      |      |      |      |      | 2(2.1%) |
| Total                                | 10   | 26   | 13   | 11   | 8    | 12   | 7    | 4    | 1    | 92(100%) |

### 3.3 Antimicrobial susceptibilities

A total of 92 strains of *E. meningoseptica* showed no drug resistance only to minocycline and showed varying degrees of resistance to the other 15 antimicrobials in seven major groups. The strains’ rate of resistance to carbapenems was
100%; the rate of resistance to cephalosporins was over 90%; that to aminoglycosides was over 80%; and that to fluoroquinolones was over 46% (Table 7).

3.4 Risk factors for *E. meningoseptica* infection

Logistic regression analysis showed that there was no statistically significant difference in BMI, age, sex, disease severity, or departmental distribution between the infected group (92 cases) and the noninfected group (184 cases) (p > 0.05), suggesting that the two sets of data are comparable (Table 4). The logistic regression analysis showed that CVC (p < 0.0001), mechanical ventilation (p = 0.015), bacteria type (p < 0.0001), operation type (p = 0.001), and fungal infection (p < 0.0001) were independent risk factors for *E. meningoseptica* infection (Table 5). The use of carbapenems (p = 0.000) and triazoles (p = 0.016) was closely related to infection with *E. meningoseptica* (Table 6). A logistic regression analysis of data from 82 patients with *E. meningoseptica* infection who had a clear outcome indicated that the type of bacteria (p = 0.037), PLT level (p = 0.014), and need for mechanical ventilation (p = 0.043) were risk factors for the death of infected patients (Table 8).

### Table 4

| Risk factors       | OR  | 95% CI       | P- Value |
|--------------------|-----|--------------|----------|
| BMI                | 1.103 | 0.781–1.556 | 0.578    |
| Grade of illness   | 1.153 | 0.403–3.303 | 0.790    |
| Age                | 0.968 | 0.928–1.009 | 0.125    |
| Sex                | 4.340 | 0.871–21.640| 0.073    |
| Department distribution | 1.001 | 0.932–1.076 | 0.968    |

NS: p ≥ 0.05

### Table 5

Independent risk factors for infection with *E. meningoseptica*

| Linear logistic regression analysis | Sex  | Age  | CVC | Mechanical ventilation | Kinds of bacteria | Operation | Fungi Infection | Grade of Illness |
|------------------------------------|------|------|-----|------------------------|-------------------|-----------|-----------------|------------------|
| Stepwise                           | p < 0.0001 | p = 0.015 | p < 0.0001 | p = 0.001 | p < 0.0001 |
| Enter                              | p < 0.0001 | p = 0.012 | p < 0.0001 | p = 0.002 | p < 0.0001 |
| Remove                             | p < 0.0001 | p = 0.002 | p < 0.0001 | p = 0.012 | p < 0.0001 |
| Backward                           | p < 0.0001 | p = 0.015 | p < 0.0001 | p = 0.001 | p < 0.0001 |
| Forward                            | p < 0.0001 | p = 0.015 | p < 0.0001 | p = 0.001 | p < 0.0001 |

NS: p ≥ 0.05
Table 6
Risk factors of *E. meningoseptica* infected analyzed by multivariate logistic regression

| Risk factors     | OR     | 95%CI       | P Value |
|------------------|--------|-------------|---------|
| β-lactam         | 0.974  | 0.387–2.455 | 0.956   |
| Carbapenem       | 5.875  | 2.895–11.923| 0.000***|
| Quinolones       | 0.658  | 0.294–1.473 | 0.308   |
| Triazoles        | 2.401  | 1.177–4.899 | 0.016** |
| Teicoplanin      | 0.692  | 0.274–1.743 | 0.434   |
| Linezolid        | 1.143  | 0.232–5.631 | 0.869   |
| Vancomycin       | 1.334  | 0.637–2.795 | 0.445   |
| Echinocandins    | 1.210  | 0.304–4.819 | 0.787   |
| Nitroimidazole   | 2.796  | 0.821–9.526 | 0.100   |
| Tetracyclines    | 2.052  | 0.794–5.303 | 0.138   |
| Other            | 4.733  | 0.389–57.643| 0.223   |

NS: p ≥ 0.05, Other included: Azithromycin (1 person-time), amphotericin B (2 person-time), clindamycin (1 person-time).
### Table 7
Antimicrobial susceptibilities of 92 *E. meningoseptica*

| Category       | Antimicrobial agent   | %R (resistance rate) | %I (intermediate rate) | %S (sensitive rate) |
|----------------|-----------------------|----------------------|------------------------|---------------------|
| Penicillin     | Piperacillin          | 36.1                 | 36.1                   | 27.8                |
|                | Piperacillin/tazobactam | 5.55                 | 20.2                   | 74.25               |
| Cephalosporin  | Ceftazidime           | 94.5                 | 0                      | 5.5                 |
|                | Cefotaxime            | 94.5                 | 0                      | 5.5                 |
|                | Cefepime              | 94.5                 | 5.5                    | 0                   |
| Cephalosporin  | Aztreonam             | 90                   | 5                      | 5                   |
| Carbapenem     | Imipenem              | 100                  | 0                      | 0                   |
|                | Meropenem             | 100                  | 0                      | 0                   |
| Aminoglycoside | Amikacin              | 80                   | 10                     | 10                  |
|                | Gentamicin            | 89.9                 | 4.6                    | 5.5                 |
|                | Netilmicin            | 88.9                 | 4.6                    | 6.5                 |
|                | Tobramycin            | 89                   | 5.4                    | 5.6                 |
| Fluoroquinolone| Ciprofloxacin         | 46                   | 13.7                   | 40.3                |
|                | Levofloxacin          | 46                   | 0                      | 54                  |
| Sulfanilamide  | Trimethoprim/         | 29.3                 | 32.8                   | 37.9                |
|                | Sulfamethoxazole      |                      |                        |                     |
| Tetracycline   | Minocycline           | 0                    | 0                      | 100                 |
Table 8
Risk factors of mortality for *E. meningoseptica* infection analyzed by multivariate logistic regression

| Risk factors          | OR    | 95%CI     | P Value |
|-----------------------|-------|-----------|---------|
| BMI                   | 1.103 | .781-1.556| .578    |
| Kinds of bacteria     | .578  | .345-.967 | .037†   |
| Grade of illness      | 1.153 | .403-3.303| .790    |
| Age                   | .968  | .928-1.009| .125    |
| WBC                   | 1.010 | .822-1.240| .928    |
| N                     | .924  | .768-1.112| .404    |
| PLT                   | 1.007 | 1.001-1.013| .014†  |
| N%                    | .956  | .773-1.182| .679    |
| N                     | .276  | .039-1.981| .201    |
| Sex                   | 4.340 | .871-21.640| .073   |
| Operation             | .912  | .194-4.294| .907    |
| mechanical ventilation| 11.191| 1.082-115.760| .043†  |
| CVC                   | 5.056 | .491-52.062| .173   |
| *Fungi Infection*     | .352  | .054-2.270| .272    |

NS: p ≥ 0.05

4 Discussion

With the continuous development of medical technology, patients in ICUs are at increasing risk of infection with *E. meningoseptica*. *E. meningoseptica* has the characteristics of multidrug resistance and strong environmental adaptability and has been considered an important infection threat for patients in critical care units[19]. This study retrieved publicly published reports related to *E. meningoseptica* from 2011 to 2019 in PubMed and retrospectively analyzed the situation of *E. meningoseptica* infection at the First Affiliated Hospital of the Third Military Medical University during the same period. The results show that the rate of *E. meningoseptica* infection has generally shown an increasing yearly trend and has affected many species across an extensive area. Epidemiological reports related to *E. meningoseptica* infection show that Taiwan had the highest number of reported cases, with a mortality rate of 63.2% [3]. Reports from South Korea, Spain, the United Kingdom, India, and Taiwan show that *E. meningoseptica* can survive in hospital sinks, faucets, humidifiers, and other ward environments and on medical equipment and can cause nosocomial outbreaks [20–23]. These findings and the broad resistance of *E. meningoseptica* in our hospital indicate that *E. meningoseptica* infection is a serious threat to people's health and lives; furthermore, the possibility that serious nosocomial infections may recur in specific populations, such as ICU patients or those with weakened immunity, cannot be ruled out. Therefore, a deeper understanding of *E. meningoseptica* is necessary.
In our study, the proportion of men infected by *E. meningoseptica* was higher than that of women, patients between 40 and 65 years old accounted for the highest proportion of infected patients (52%), and the detection rate of *E. meningoseptica* infection was significantly higher among patients in ICUs than among those in other departments. This may be related to the fact that these patients are more likely to undergo invasive procedures, require mechanical ventilation, acquire multiple bacterial infections during hospitalization, and develop combined fungal infections. The logistic analysis also showed that these factors were high risk factors for *E. meningoseptica* infection. A number of studies focusing on infections caused by *E. meningoseptica* have reported that prolonged hospital stays, CVC, invasive procedures, and the use of broad-spectrum antimicrobials are the main risk factors for *E. meningoseptica* infection and related death [24]. In addition, low immunity is also a risk factor for *E. meningoseptica* infection [3]. A decline in PLT levels is often related to disease severity [25]. Patients in ICUs are more severely ill, have lower immunity and have a higher incidence of reduced PLT and therefore are more susceptible to *E. meningoseptica* infection. In this regard, our finding is consistent with the results reported in the literature. The research results also provide a reminder that when treating high-risk patients, we should minimize procedures such as mechanical ventilation and CVC, strengthen hand hygiene management and aseptic surgical practices, provide immune support treatments to improve patients’ immunity, prevent fungal infections, and provide timely treatment for infections that do arise. Such measures may help reduce the risk of *E. meningoseptica* infection and the likelihood of nosocomial outbreaks.

In this study, the *E. meningoseptica* detection rate was the highest in patients undergoing brain surgery. Most of the patients had been treated with carbapenems, and antimicrobial susceptibility test results showed that the resistance rate of *E. meningoseptica* to carbapenems was 100%. To better explain this phenomenon, we consulted a large number of studies and found that although carbapenems have strong antibacterial activity against gram-negative bacteria, *E. meningoseptica* is the only known microorganism to have two chromosomes that inherently carry MBL genes and can develop resistance to a variety of antimicrobials that target gram-negative bacteria[26]. The MBL genes are resistant to class B metallo-β-lactamases. The β-lactamase-resistant genes that have been confirmed in *E. meningoseptica* include CME, blaB and GOB; among these, blaB is directly related to imipenem resistance, and the expression of this gene is elevated in the cerebrospinal fluid during *E. meningoseptica* infection [27]. In addition, the MBL genes can spread horizontally in the genetic elements of conditional pathogens similar to *Enterobacter*, leading to a widespread increase in drug-resistant bacteria[28]. Meningitis, bloodstream infection and lung infection caused by *E. meningoseptica* present great difficulties for clinical treatment. The high mortality rate of *E. meningoseptica* infection is also closely related to the multidrug resistance of the bacteria [29]. With the continuous emergence of drug-resistant strains, the rational use of antimicrobials is particularly important. Researchers are also continuously trying different regimens to treat *E. meningoseptica* infection. Indian scholars have reported that the intrathecal injection of tigecycline and vancomycin to treat meningitis caused by *E. meningoseptica* has had good therapeutic effects. However, when vancomycin is used to treat hemodialysis patients, its efficacy is reduced, and although vancomycin can be combined with ciprofloxacin, linezolid, or rifampicin, it is necessary to pay close attention to antimicrobial susceptibilities by using the correct drug susceptibility testing method [30]. Nonetheless, due to delays in reporting time caused by differences in pathogenic microorganism detection methods, empirical use of antimicrobials still occurs in a broad range of practices. The results of this study indicate that for patients with suspected *E. meningoseptica* infection, carbapenems, cephalosporins, aminoglycosides, and fluoroquinolones should be avoided, and minocycline is recommended as an empirical anti-infective treatment. However, we should also collect samples of infected foci whenever possible for pathogenic microorganism monitoring and drug susceptibility testing and should adjust anti-infection treatment plans in a timely manner based on drug susceptibility test results.

In its analysis of the global epidemiological characteristics of *E. meningoseptica*, this study only searched the large and widely used PubMed database and did not search other databases. Some related papers might be missing, resulting in incomplete data. In addition, the main conclusions of this study are based on a single-center retrospective analysis, and
the sample size is relatively small. Some patients stopped treatment at our hospital, and we failed to effectively follow up to determine whether they died due to *E. meningoseptica* infection. Therefore, some conclusions of the study may be biased, and more large-scale, large-sample clinical analyses are needed for further confirmation.

5 Declarations

Ethics approval

This study was approved by the Ethics Committee of the First Affiliated Hospital of the PLA Military Medical University. Ethics NO. KY2020296.

Consent for publication

Yes.

Availability of data and materials

Data and materials are publicly available

Declaration of Competing Interests

We declare no conflicts of interest.

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Author Contributions

Yali Gong: acquisition of data, drafting the article, the conception and design of the study, final approval of the version to be submitted. Xiaoqiang Luo: acquisition of data, final approval of the version to be submitted. Yuan Peng: acquisition of data, final approval of the version to be submitted. Cheng Zhang: acquisition of data, final approval of the version to be submitted. Ming Li: acquisition of data, final approval of the version to be submitted. Ning Li: analysis and interpretation of data, final approval of the version to be submitted. Qimeng Li: analysis and interpretation of data, final approval of the version to be submitted. Yulong Shi: analysis and interpretation of data, the conception and design of the study, final approval of the version to be submitted. Siyuan Ma: the conception and design of the study, revising the article critically for important intellectual content, final approval of the version to be submitted.

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