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Original Article

Risk factors for death from *Stenotrophomonas maltophilia* bacteremia☆

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ABSTRACT

Purpose: *Stenotrophomonas maltophilia* has low pathogenicity potential, but if it causes bacteremia it can be fatal, because it has shown high resistance to many antibiotics and can be difficult to treat. Patient death from *S. maltophilia* bacteremia has increased since 2014 in our hospital. In this study, we investigated risk factors for death due to *S. maltophilia* bacteremia.

Methods: Seventy patients from the hospital database with *S. maltophilia* bacteremia between January 2010 and July 2017 were investigated. We retrospectively analyzed risk factors including gender, age, wards, hospitalized duration, clinical history, devices, source of *S. maltophilia* identification, polymicrobial bacteremia, prior antimicrobial therapy, antimicrobial therapy after bacteremia, and resistance to antibiotics. The statistical analysis was performed to compare the period from 2010 to 2013 to from 2014 to 2017.

Results: Comparing the 2010–2013 period to the 2014–2017 period, it revealed that history of hospitalization, identification of *S. maltophilia* from sputum, polymicrobial bacteremia, prior carbapenem use, and mortality was significantly different in *S. maltophilia* bacteremia ($p = 0.028$, $p = 0.004$, $p < 0.001$, $p = 0.034$, and $p = 0.007$, respectively). Comparison between non-survivors and survivors for 2010–2013 and 2014–2017 found ICU admission and ventilator use were seen more often in non-survivors ($p = 0.030$ vs $p = 0.013$ and $p = 0.027$ vs $p = 0.010$, respectively).

Conclusions: Our analyses showed increase in mortality from *S. maltophilia* bacteremia from 2014 to 2017, and that non-survivors had a higher frequency of ICU admission and ventilator use in both the 2010–2013 and 2014–2017 periods. There were more combination antimicrobial therapy cases after bacteremia in 2014–2017. Further prospective studies with larger numbers of patients should be undertaken for definitive conclusions.

1. Introduction

Stenotrophomonas maltophilia demonstrates intrinsic resistance to multiple antibiotics including β-lactams, quinolones and aminoglycosides. Cases with bacteremia may have a poor prognosis [1]. Despite fatalities, few studies have been performed in comparison with other kinds of Gram-negative bacteria such as *Pseudomonas* [2]. *S. maltophilia* is quite important as a nosocomial infection-causative bacteria. *S. maltophilia* is an opportunistic pathogen for nosocomial infection, and the 3rd most frequently isolated bacteria in large scale surveillance studies of bacteremia patients [3,4].

The first choice among recommended antibiotics is Trimethoprim- Sulfamethoxazole (TMP-SMX), rather than more frequently

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used agents in urinary tract infection (UTI) field such as β-lactams or aminoglycosides [1]. Initiation of appropriate therapy may tend to be delayed, resulting in high mortality rates (21–69%) [5]. There are few studies of the clinical risk factors for *S. maltophilia* infection, although it is recognized as a problem in intensive care unit (ICU) hospitalized patients [6].

Known risk factors for *S. maltophilia* infection include inappropriate antimicrobial treatments, broad-spectrum treatments, prolonged hospitalization, ICU admission, and ventilation [6–8]. These risk factors were associated with mortality in *S. maltophilia* infections [7]. Most studies, however, were of specific populations, such as cancer and ICU patients, and included carrier and infected patients [9].

After finding an increase in fatalities associated with *S. maltophilia* infections in our hospital since 2014 (Fig. 1), we studied the possible risk factors for mortality in *S. maltophilia* bacteremia between cases from 2010–2013 and 2014–2017. We performed a preliminary case-control study in preparation for a future cohort investigation of the risk factors for fatality in *S. maltophilia* bacteremia patients.

2. Patients and methods

2.1. Patients

We gathered the data from consecutive patients with *S. maltophilia* bacteremia caused by nosocomial infection from January 2010 to July 2017 from the hospital database. Data from patients with polymicrobial bacteremia were also included. This study was approved by the institutional review board of Kobe University (No. 472-3, Kobe University Graduate School of Health Sciences).

2.2. Potential risk factors

As potential risk factors for death from *S. maltophilia* bacteremia, we included the following variables: gender; age; underlying diseases (cardiovascular disease and malignancy including solid and hematologic); wards (cardiology, gastroenterology, pediatrics, respiratory medicine, others); ICU admission; contact precautions; hospitalized duration; clinical histories (hospitalization, hemodialysis, surgery, transplantation); devices (urinary tract catheter or stent, intravenous hyperalimentation, or ventilator); *S. maltophilia* identification from sputum (prior to or after isolation from blood) or other materials; polymicrobial bacteremia; prior antimicrobial therapies [carbapenems (meropenem or doripenem)], piperacillin-tazobactam and fluoroquinolones (ciprofloxacin, levofloxacin, or pazufloxacin)]; antimicrobial therapies after bacteremia (combination therapy, monotherapy and no specific therapy) and use of the antibiotics minocycline (MINO), TMP-SMX, and fluoroquinolone (ciprofloxacin or levofloxacin (LVFX)). 'Wards' refers to the ward where the patient was staying when the bacteria were isolated. *S. maltophilia* resistance to ceftazidime, LVFX, MINO and TMP-SMX was tested. Patient history data were studied for the 3 months prior to isolation of *S. maltophilia* bacteremia. Mortality by *S. maltophilia* bacteremia was defined as death within 60 days after the bacteremia isolation with no other apparent cause of death. Our study period of up to 60 days after *S. maltophilia* bacteremia was diagnosed is longer than that of previous studies, which ranged from 28 to 30 days [10,11].

2.3. Microbiological definitions

S. maltophilia bacteremia was defined using the BacT/ALERT system (SYSMEX bioMérieux Co., Ltd., Tokyo, Japan). Bacterial identification and antimicrobial susceptibility tests were performed using WalkAway (Beckman Coulter, Inc., Tokyo, Japan) and MALDI Biotyper (Bruker Daltonics K.K., Yokohama, Japan). Antimicrobial susceptibility was determined using the breakpoints categorized by the 2012 Clinical and Laboratory Standards Institute (CLSI) [12].

2.4. Statistical analysis

We conducted univariate analyses of the variables between the 2010–2013 and 2014–2017 groups, and between non-survivors and survivors, using SPSS statistical software ver. 24 (SPSS Japan Inc., Tokyo, Japan). Comparison of median values was done by Mann-Whitney *U* test and other comparisons used Fisher's direct exam or chi-squared test. All *p* values of 0.05 or less were considered to be statistically significant.

3. Results

3.1. Patients

Seventy patients had *S. maltophilia* bacteremia in the study period. We found an increase in death from *S. maltophilia* infection from 2014–2017 in the cases of *S. maltophilia* bacteremia in our hospital between 2010 and 2017 (Fig. 1). The details are shown in Table 1. Of 34 males and 36 females, there were 24 non-survivors (34.3%) and 46 survivors (65.7%) of *S. maltophilia* bacteremia (Table 1). There were 17 (50.0%) non-survivors from 2014–2017 compared to 7 (19.4%) from 2010–2013 ($p = 0.007$).

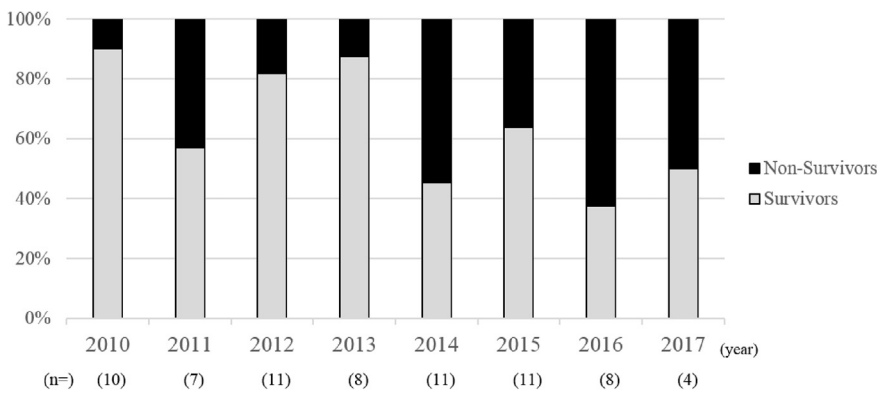

Fig. 1. Increased mortality from *Stenotrophomonas maltophilia* bacteremia between 2010 and 2017.

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