J Infect Chemother xxx (2017) 1–6

Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

journal homepage: http://www.elsevier.com/locate/jic

Original Article

Etiology of community-onset monomicrobial bacteremic pneumonia and its clinical presentation and outcome: *Klebsiella* and *Pseudomonas* matters

Chao-Yung Yang [a], Chung-Hsun Lee [a, b], Chih-Chia Hsieh [a], Wen-Chien Ko [b, c, **], Ching-Chi Lee [a, c, d, e, *]

[a] Department of Emergency Medicine, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan 70403, Taiwan
[b] Department of Medicine, College of Medicine, National Cheng Kung University, 70403, Tainan, Taiwan
[c] Department of Internal Medicine, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan 70403, Taiwan
[d] Division of Critical Care Medicine, Department of Internal Medicine, Madou Sin-Lau Hospital, Tainan 72152, Taiwan
[e] Graduate Institute of Medical Sciences, College of Health Sciences, Chang Jung Christian University, Tainan 71101, Taiwan

ARTICLE INFO

Article history:
Received 11 May 2017
Received in revised form
10 August 2017
Accepted 31 August 2017
Available online xxx

Keywords:
Community
Bacteremic pneumonia
Pseudomonas species
Klebsiella species

ABSTRACT

To describe the difference of the clinical features, bacteremia severity, and outcome of patient with community-onset bacteremic pneumonia between *Pseudomonas, Klebsiella,* and other causative microorganisms, the total 278 adults with community-onset monomicrobial bacteremic pneumonia were studied in a retrospective cohort. *Klebsiella* (61 patients, 21.9%) and *Pseudomonas* (22, 7.9%) species was the leading and the fifth common pathogen, respectively. More patients having initial presentation with critical illness (a Pitt bacteremia score $\geq$ 4) and a fatal comorbidity (McCabe classification) as well as a higher short- (30-day) or long-term (90-day) mortality rate was evidenced in patients infected with *Klebsiella* or *Pseudomonas* species, compared to other causative microorganisms. Compared to patients in the *Klebsiella* group, more frequencies of recent chemotherapy and an initial presentation of febrile neutropenia, and less proportions of diabetes mellitus were disclosed among those in the *Pseudomonas* group. Of importance, a significantly differential survival curve between *Klebsiella* or *Pseudomonas* species and other species during 30-day or 90-day period after bacteremia onset but a similarity of *Pseudomonas* and *Klebsiella* species was evidenced, using the Cox-regression after adjusting the independent predictors of 30-day mortality. Conclusively, of pathogens causing community-onset bacteremic pneumonia, *Klebsiella* and *Pseudomonas* species should be recognized as the highly virulent pathogens and resulted in poor short- and long-term prognoses.

1. Introduction

Despite improvements in hemodynamic support and antibiotic therapy, bacteremia remains associated with high morbidity and mortality, which contribute substantially to health care costs [1]. Community-onset bacteremia, which a population-based study reported to have an annual incidence of 0.82%, is a common problem for clinicians [2], and bacteremic pneumonia was frequently linked to poor prognosis [3,4].

Klebsiella pneumoniae is the major cause of community-acquired pyogenic infections worldwide [5,6], and the global variations in clinical patterns have been discussed [5]. *K. pneumoniae* constitutes a part of the pneumonia-causing microorganisms worldwide [6,7], particularly in Taiwan [8]. More importantly, *K. pneumoniae* has been strongly associated with severe pneumonia episodes [8], which are generally recognized as an independent risk factor for

* Corresponding author. Department of Critical Care Medicine, Madou Sin-Lau Hospital, No. 20, Lingzilin, Madou Dist., 72152, Tainan City, Taiwan.
** Corresponding author. Division of Infectious Disease, Department of Internal Medicine, National Cheng Kung University Hospital, No. 138, Sheng Li Road, 70403, Tainan, Taiwan.
E-mail addresses: winston3415@gmail.com (W.-C. Ko), chichingbm85@gmail.com (C.-C. Lee).

http://dx.doi.org/10.1016/j.jiac.2017.08.019
1341-321X/

mortality in pneumonic patients [9], especially for alcoholic patients [10].

Community-acquired *Pseudomonas* pneumonia is rare, with the majority of patients having pre-existing diseases including malignancy, cystic fibrosis, aplastic anemia, chronic obstructive pulmonary disease, and bronchiectasis [11]. However, its incidence increases with the augmentation of pneumonia severity; thus *Pseudomonas* remains the leading pathogen in pneumonic patients requiring intensive care unit (ICU) admission [12,13]. With regard to the relation of these two pathogens linked to severe pneumonia, no study has described the differences in clinical manifestations and outcomes, and this knowledge would be helpful to the admitting physician in making treatment decisions before the results of laboratory cultures become available. Therefore, we undertook an investigation to compare the clinical features, pneumonia severity, and patient outcomes for community-onset monomicrobial bacteremic pneumonia caused by varied pathogens, particularly in *Pseudomonas* and *Klebsiella* species.

2. Materials and methods

2.1. Study design

This retrospective cohort study was conducted during the 6-year period between January 2008 and December 2013 at the emergency department (ED) of the medical center located in Southern Taiwan. The study hospital is a tertiary-care, 1200-bed, university-based medical center with approximate annual ED visits of 70,000 patients. The study was approved by the institutional review board, and the requirement for informed consent was waived. This information was collected and studied using the format recommended by STROBE [14]. Partial clinical information in this study cohort has been published [4,15–18].

Among adults with blood cultures sampled in the ED during the study period, bacterial growth in blood cultures was screened in a computer database in the study hospital. Of adult patient with the growth of blood culture, those with community-onset bacteremia were studied after exclusion of those with contaminated blood cultures, incomplete chart records, hospital-onset bacteremia, or in whom bacteremia was diagnosed prior to the ED visits. Among patients having community-onset bacteremia, those were included in the study if patients met all the following criteria: signs or symptoms of pneumonia on admission (*e.g.*, fever, cough, sputum, and rales) and roentgenographic evidence of pneumonia within the first three days of ED arrival.

Clinical information was retrieved from medical records in patients with community-onset bacteremia and only those having monomicrobial bacteremia because of pneumonia were collected. Using a predetermined case record form, their demographic data (such as age, sex, and place of residence), comorbidities, initial syndromes (severe sepsis and septic shock), vital signs, consciousness level, antimicrobial agents, and laboratory data were collected within 24 h after ED arrival. Furthermore, causative microorganisms, susceptibility results, duration and type of antimicrobial agents, recent hospitalizations, prior antimicrobial use, recent events (such as invasive procedures, chemotherapy, radiotherapy, and/or surgery) performed during the four weeks before ED arrival, and clinical outcome, were also recorded. Two authors reviewed medical records of eligible patients for the above clinical information. If any discrepancies were observed, both authors inspected medical records simultaneously and a decision was reached through consensus. Only the first episode of each patient, if there were multiple bacteremic episodes, was included.

The primary and secondary endpoint was 30-day and 90-day mortality, respectively. To avoid underestimating the 90-day mortality rate, if a patient was not followed up at the outpatient clinic after discharge, outcome information was retrieved by telephone contact. Patients unable to be reached by telephone were excluded.

2.2. Microbiological methods

Bacteremic aerobic isolates in the study period were prospectively collected. Bacteremic isolates were identified by the GNI Card of the Vitek system (bioMe'rieux, Lyon, France). Antimicrobial susceptibility was determined by the disk diffusion method, based on performance standards of the Clinical Laboratory Standard Institute (CLSI) in 2016 [19]. For Gram-negative bacilli, the tested drugs included cefazolin, cefuroxime, cefotaxime, ceftazidime, cefepime, and levofloxacin. For streptococci, the tested drugs included cefotaxime, cefepime, ertapenem, and levofloxacin. Cefoxitin was tested for *Staphylococcus aureus* isolates for identification of methicillin-resistant *S. aureus* (MRSA). If a patient was empirically treated by other agents, the susceptibility of the specific drug was measured.

2.3. Definitions

Community-onset bacteremia indicates that the place of onset of the bacteremic episode is the community, and includes long-term health-care facilities- and community-acquired bacteremia, as previously described [4,15–18]. Blood culture samples with potential contaminating pathogens were regarded as being contaminated, according to previously described criteria [20]. Polymicrobial bacteremia was defined as the isolation of more than one microbial species from a single bacteremic episode; otherwise, the episode was regarded as monomicrobial bacteremia. Febrile neutropenia was defined as fever and an absolute neutrophil count <500 cells/mm^3.

As previously described [4,17,18], the antimicrobial therapy was considered appropriate when all the following criteria were fulfilled: (i) the route and dosage of antimicrobial agents were administered as recommended in the Sanford Guide [21]; (ii) bacteremic pathogens were *in vitro* susceptible to the administrated antimicrobial agent based on the contemporary CLSI breakpoints [19]. As previous definitions [18], inappropriate empirical antibiotic therapy was defined as the time-to-appropriate antibiotic of >48 h and the elapsed time was defined as the period between the ED arrival (*e.g.*, ED triage) and the administration of appropriate antimicrobials. The bacteremia severity was graded by the Pitt bacteremia score [4], and those with a high Pitt bacteremia score ($\geq$4) was indicated as being critically illness. Comorbidities were defined as previous reports [22] and malignancies included hematological malignancies and solid tumors. The severity of underlying diseases was assessed by a previously delineated McCabe classification system [23].

2.4. Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences for Windows (Chicago, Illinois, USA), Version 20.0. A univariate analysis for the predictors of 30-day mortality was studied by a Chi-square test or Fisher's exact test. To assess the independent predictors of with adjusted odds ratios, all variables of 30-day mortality with a P value less than 0.1 in the univariate analysis were included in a stepwise and backward multivariable logistic regression model. Cox regression and Kaplan-Meier survival curves were used to compare the effects of causative microorganism on clinical outcomes, after adjustment for independent

Please cite this article in press as: Yang C-Y, et al., Etiology of community-onset monomicrobial bacteremic pneumonia and its clinical presentation and outcome: *Klebsiella* and *Pseudomonas* matters, J Infect Chemother (2017), http://dx.doi.org/10.1016/j.jiac.2017.08.019