J Infect Chemother 21 (2015) 531–537

Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

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

Original article

Influence of the bacterial phenotypes on the clinical manifestations in *Klebsiella pneumoniae* bacteremia patients: A retrospective cohort study☆

Atsushi Togawa [a, *], Hiromi Toh [b], Kyoko Onozawa [c], Michinobu Yoshimura [a], Chiemi Tokushige [b], Nobuyuki Shimono [c], Tohru Takata [a], Kazuo Tamura [a]

[a] Division of Medical Oncology, Hematology, and Infectious Diseases, Department of Medicine, Fukuoka University, Japan
[b] Division of Microbiology Laboratory, Fukuoka University Hospital, Japan
[c] Department of Internal Medicine I, Kyushu University, Japan

ARTICLE INFO

Article history:
Received 15 December 2014
Received in revised form
9 March 2015
Accepted 8 April 2015
Available online 22 April 2015

Keywords:
Klebsiella pneumoniae
Bacteremia
Septic shock
Liver abscess
Mortality

ABSTRACT

Ninety-four episodes of *Klebsiella pneumoniae* bloodstream infection were identified at a university hospital in Japan. After excluding extended-spectrum beta lactamase-producing strains, 83 blood isolates from these patients were assayed in terms of their bacterial phenotypes such as the mucoid and hypermucoviscosity phenotypes. Bacterial phenotypes were correlated with the patients' clinical manifestations. The hypermucoviscosity phenotype was significantly associated with septic shock at the onset of infections (odds ratio, 15.92; 95% confidence interval, 1.27–468.12), but was not associated with liver abscess formation. Mortality was determined by the presence of septic shock. *RmpA* gene was associated with the induction of the hypermucoviscosity phenotype. These results reveal unique roles of bacterial phenotypes on the patient's clinical condition in *K. pneumoniae* bacteremia.

© 2015, Japanese Society of Chemotherapy and The Japanese Association for Infectious Diseases. Published by Elsevier Ltd. All rights reserved.

1. Introduction

Klebsiella pneumoniae is one of the most common pathogenic bacteria. It has been known to be a common hospital-acquired pathogen, causing diseases such as pneumonia, urinary tract infection, and intra-abdominal infection in patients whose immunity is compromised by underlying diseases such as diabetes mellitus [1]. It has also been recognized as a possible pulmonary pathogen causing community-acquired pneumonia with symptoms such as high fever, hemoptysis, and lung abscess formation [2]. However, the incidence of community-acquired *Klebsiella* pneumonia has substantially declined over the decades in developed countries [3].

A distinctive invasive syndrome with pyogenic liver abscess formation has started to be described in literature from Taiwan in 1980s [4,5]. Extrahepatic complications resulting from bacteremic dissemination, including endophthalmitis [5], meningitis [6], and necrotizing fasciitis [7] have also been reported. The invasive syndrome was subsequently reported in many Southeast Asian countries, including Singapore [8], Hong Kong [9], and Korea [10].

The pathogenesis of this invasive syndrome has been extensively investigated. Expression of capsular serotypes K1 and K2 are considered to be the predominant virulence factors of *K. pneumoniae* infections [11]. Furthermore, K1 has been shown to be the most common serotype isolated from patients with *K. pneumoniae* liver abscess and endophthalmitis [12]. Mucoviscosity has also been documented as a virulence factor of *K. pneumoniae* [11,13], and *magA* gene is shown to be involved in the hypermucoviscosity phenotype [14]. A high prevalence of *magA* gene has been found among pyogenic liver abscess-associated *K. pneumoniae* strains [14,15]. Furthermore, it has been demonstrated that *magA* gene is responsible for the expression of capsular serotype K1 [16], which determines the hypermucoviscosity phenotype of bacterial strain and is strongly associated with pyogenic liver abscess formation in *K. pneumonae* patients [17]. Another report also demonstrated that serotype K1 was associated with septic ocular or central nervous system complications from

☆ This paper was recommended for submission to this journal by chairperson at the conference of the 88th Annual Conference of The Japanese Association for Infectious Diseases.

* Corresponding author. Division of Medical Oncology, Hematology, and Infectious Diseases, Department of Medicine, Fukuoka University, 7-45-1 Nanakuma, Jonan-ku, Fukuoka 8140180, Japan. Tel.: +81 092 801 1011; fax: +81 092 865 5656.
E-mail address: atogawa@fukuoka-u.ac.jp (A. Togawa).

http://dx.doi.org/10.1016/j.jiac.2015.04.004
1341-321X/© 2015, Japanese Society of Chemotherapy and The Japanese Association for Infectious Diseases. Published by Elsevier Ltd. All rights reserved.

pyogenic liver abscess independent of underlying diseases in the host [18].

Analysis of 455 episodes of *K. pneumoniae* bloodstream infections from seven countries, which did not include Japanese patients, revealed a divergent trend of virulence characteristics and clinical manifestations among countries [19,20]. Among 204 bacterial strains isolated, hypermucoviscosity phenotype was detected in 37% of blood isolates. Interestingly, 52% and 50% of blood isolates from Taiwan and South Africa, respectively, were positive for this phenotype, whereas only 5% of those from the rest of the world was positive. This phenotype was detected in 68% and 100% of patients with community-acquired pneumonia and invasive syndrome including liver abscess, endophthalmitis, and meningitis in Taiwan and South Africa, respectively. *RmpA* gene, which is also associated with the presence of hypermucoviscosity phenotype, was positive in 86% of hypermucoviscous blood isolates, but only in 7% of non-hypermucoviscous blood isolates.

Since Japanese patients were not involved in this study, the precise virulence factor of *K. pneumoniae* bacteremia and its relationship with the presence of invasive syndrome in cases from Japan were not described. Similar study involving Japanese patients was hard to find, except some case reports [21]. In this report, we analyzed 73 episodes of non-ESBL producing *K. pneumoniae* bloodstream infections to elucidate the clinical manifestations of *K. pneumoniae* bacteremia in Japanese population.

2. Methods

2.1. Study design

A retrospective study of patients with *K. pneumoniae* bacteremia was conducted in a university hospital in Fukuoka, Japan. The study period was from January 1, 2009, to August 31, 2013. All patients were of Japanese ethnicity. Bacterial phenotypes were investigated and genetic analyses were performed in microbiology laboratories of two universities. Clinical manifestations were determined from medical charts. The study was observational in that administration of antimicrobial agents and other therapeutic management were controlled by the patient's physicians, not by the investigators, except in cases when intervention by infectious disease physician was performed.

2.2. Definitions

Terms were defined before the study was started. Type of infections was defined as community-acquired and hospital-acquired, in which bacteremia was detected within 48 h of admission in the former type of infection. Septic shock was defined as septic syndrome with lowered blood pressure, i.e. systolic blood pressure <90 mmHg. Liver abscess was defined by evidence of intrahepatic abscess formation by computed tomography or magnetic resonance imaging scan. Diabetes mellitus was defined by evidence of elevated blood glucose and/or HbA1c as reported previously [22]. Site of infections accompanying the bacteremia was determined as urinary tract infection, biliary tract infection, and pneumonia. Cholecystitis and/or cholangitis were included in biliary tract infection, excluding liver abscess. Mortality was defined by death of any cause within 30 days from the onset of symptoms.

2.3. Microbiology

Each blood isolate was identified as *K. pneumoniae* by using Vitek II system (SYSMEX bioMerieux, Tokyo, Japan). The isolates were frozen at −80 °C until analysis.

The isolates were initially classified phenotypically as mucoid or non-mucoid. When isolates were plated on deoxycholate hydrogen sulfide lactose (DHL) agar, isolates with mucoid phenotype showed greasy colonies with no apparent boundary formation between colonies, whereas isolates with non-mucoid phenotype showed less greasy colonies with visible boundary between colonies (Fig. 1). On isolates with mucoid phenotype, string test was performed accordingly to determine the presence of hypermucoviscosity phenotypes [14]. String test was not performed on nonmucoid isolates because these isolates did not possess hypermucoviscosity (unpublished data). A standard bacteriologic loop was used to stretch a mucoviscous string from the colony. Hypermucoviscosity was defined by the formation of viscous strings >5 mm in length when a loop was used to stretch the colony on agar plate (positive string test). Presence of *magA* and *rmpA* genes was determined by using bacterial DNAs with polymerase chain reaction. The primer sequences for PCR reactions were as follows: for the amplification of *magA* gene, [GGTGCTCTTTACATCATTGC] and [GCAATGGCCATTTGCGTTAG], yielding 1283bp DNA fragments; for the amplification of *rmpA* gene, [ACTGGGCTACCTCTGCTTCA] and [CTTGCATGAGCCATCTTTCA], yielding 536bp DNA fragments. The thermal cycle condition was 94 °C for 120 s, then 35 cycles of 94 °C for 60sec, 55 °C for 60sec, and 72 °C for 60 s, with the final step of 72 °C for 7 min. Amplified samples were kept at 4 °C until analysis.

2.4. Statistics

Patient demographics and laboratory data were processed by JMP software ver. 10 (SAS Institute Japan, Tokyo, Japan). The Pearson $\chi 2$ test was used to compare categorical variables. Logistic regression analyses were used to determine which risk factors were statistically significant for each clinical manifestation.

3. Results

During the study period, a total of 94 *K. pneumoniae* blood isolates were identified, of which 11 isolates were further determined to be extended-spectrum beta-lactamase (ESBL) -producing strains. ESBL-producing isolates were excluded from the study since their virulence factors and clinical manifestations might be different from non-ESBL-producing isolates. The remaining 83 non-ESBL-producing blood isolates were classified by the type of infections. Thirty-two blood isolates were determined as community-

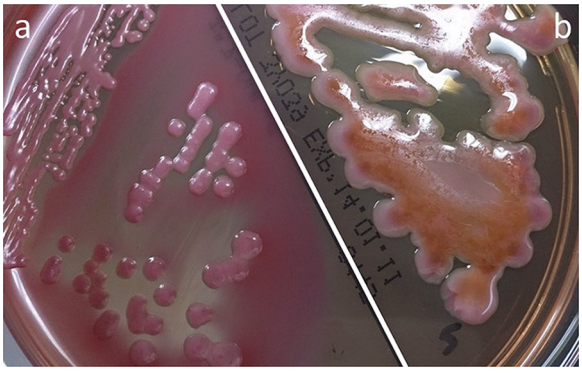

Fig. 1. Morphology of non-mucoid and mucoid K. pneumonia blood isolates on DHL agar. Blood isolates were cultured on DHL agar for three days and photographed. Blood isolates with non-mucoid phenotype (a) showed greasy appearance with visible boundary in smaller colonies, whereas those with mucoid phenotype (b) completely lack boundary between colonies.

Download English Version:

https://daneshyari.com/en/article/3376844

Download Persian Version:

https://daneshyari.com/article/3376844

Daneshyari.com