Clinical Features and Development of Sepsis in Klebsiella Pneumoniae Infected Liver Abscess Patients: A Retrospective Analysis of 135 Cases

Shixiao Li
Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University

Sufei Yu
Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University

Minfei Peng
Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University

Jiajia Qin
Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University

Chunyan Xu
Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University

Jiao Qian
Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University

Minmin He
Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University

Peng Zhou (zhoupeng198118@126.com)
Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University

Research Article

Keywords: Pyogenic liver abscess, Klebsiella pneumoniae, Sepsis, Metastatic infection

DOI: https://doi.org/10.21203/rs.3.rs-154544/v1

License: © This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Background

*Klebsiella pneumoniae* is a primary pathogen of pyogenic liver abscess (PLA). However, little data are available on combination with sepsis. In this study, we aimed to evaluate the clinical characteristics and prognostic differences of PLA patients with sepsis.

Methods

This retrospective cohort study was conducted to investigate 135 patients with confirmed *Klebsiella pneumoniae*-caused liver abscesses (KPLA) from a tertiary teaching hospital, from 2013 to 2019. The patients were divided into two groups based on comorbidity with sepsis. The demographic characteristics, clinical features as well as laboratory and microbiologic findings was analyzed.

Results

The 135 patients were analyzed, with a mean age of 60.9 ± 12.7 years, and 59.3% were men. Among them, 37/135 (27.4%) had comorbid sepsis and mortality rate was 1.5%. The most common symptom was fever (91.1%). KPLA patients with sepsis had a significantly higher proportion of frailty, diarrhea, fatty liver, chronic renal insufficiency, and hepatic dysfunction (p < 0.05). Antibiotic therapy and percutaneous drainage were most frequently used. The incidences of sepsis shock, acute respiratory distress syndrome was higher in the sepsis group compared to the non-sepsis group. As for metastatic infections, the lung was the most common site. Respiratory symptoms were found in 11 patients, and endophthalmitis coexisted in 4 patients, and meningitis occurred in 1 patient.

Conclusion

Our findings emphasize that KPLA patients combined with and without sepsis have different clinical features, but KPLA patients with sepsis have a high rate of complications and metastatic infections. Further surveillance and control of septic spread is essential in KPLA patients.

Introduction

Pyogenic liver abscess (PLA) is a common intraabdominal infectious disease, which is caused by various bacteria. Recent findings showed a much higher incidence of PLA in Taiwan (17.6 per 100,000 individuals) than that in northeast China (5.7 per 100,000 individuals), and the United States (3.59 per 100,000 individuals)[1]. With the recent advances in diagnostic and therapeutic capability, the fatality rate has gradually declined (7.8% to 28.6%)[2]. In the past two decades, *Klebsiella pneumoniae* has been identified as the predominant pathogen of PLA in Asia[3]. *Klebsiella pneumoniae*-caused liver abscess (KPLA) was first reported in the 1980s in Taiwan[4], and the incidence rate of KPLA was from 30% in the 1980s to over 80% in the 1990s[5]. Recently, KPLA has been extensively described in mainland China and other countries including America, and Europe[6-8].

*Klebsiella pneumoniae* can colonize the intestine and penetrate the intestinal mucosal barrier in pathological states to enter the liver via the portal vein system and subsequently cause KPLA[3]. KPLA often has a poor prognosis, particularly among those with metastatic infection, including bacteremia, meningitis, endophthalmitis, and other extrahepatic infections[8, 9]. Research suggests that the rate of metastatic infection has a range of 3.5%–20%, and the mortality rate of patients with KPLA is 2.8%-10.8%[10]. Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to an infection, with unacceptably high morbidity and mortality[11]. Sepsis is a common and serious complication in patient with PLA[12]. The delay to diagnose and treatment for PLA in timely in patients with initially stable hemodynamics can result in rapid progression to sepsis. Sepsis can lead to organ dysfunction and eventually death.

Unfortunately, little is known about clinical features and the incidence of *K. pneumoniae* causing PLA with sepsis in the Eastern China. Therefore, this study was undertaken to summarize the clinical and microbiologic characteristics, metastatic infection of KPLA patients with and without sepsis.

Methods

Study design

This study was a retrospective review of all patients who were diagnosed as having KPLA infection (International Classification of Disease, Clinical Modification 572.0) and hospitalized in the Taizhou Hospital of Zhejiang Province, a 1500-bed tertiary teaching hospital located in east China, from January 2013 to December 2019. The KPLA diagnosis was based on the combination of presence of the typical clinical symptoms, such as fever, chills, right upper abdominal pain, imaging examinations of the abscess cavity in the liver as diagnosed by abdominal ultrasonography (US) and/or computerized tomography (CT) and culture identified with *K. pneumoniae* isolated from the blood or pus samples. In this study, the patients who did not have clear records or did not finish the treatment were excluded. The inclusion criteria of sepsis were evaluated with the SOFA scores higher than or equal to 2[13]. Sepsis was defined as infection associated with at least 2 of the following[4-14]: (1) fever (rectal temperature of ≥38.3°C); (2) hypothermia (core temperature < 35.6 °C); (3) respiratory rate >20 bpm or PaCO₂ <32 mmHg; (4) tachycardia (heart rate>90 bpm); (5) altered mental status; (6) significant edema or positive fluid balance (>20 mL/kg during 24 h). Metastatic infection was defined as infection associated with liver abscess developed extrahepatic complication such as endophthalmitis,
central nervous system infections, lung abscesses, and skin or soft tissue infections. This study protocol was approved by the Institutional Medical Ethics Committee of Taizhou Hospital of Zhejiang Province. Due to the retrospective nature of the study, the need for informed consent was waived.

Microbiologic data

Pus and / or blood were collected for culture. The VITEK 2 compact system (bioMérieux Vitek Inc., France) was used for the identification of the 135 K. pneumoniae strains. The antimicrobial resistance of strains was detected by antimicrobial sensitivity tests which were done by VITEK 2 Compact and disc diffusion method on the Mueller-Hinton (MH) Agar plates. All laboratory tests were performed according to ISO 15189:2012 standards. The antimicrobial susceptibility was interpreted according to the Clinical and Laboratory Standards Institute guidelines (CLSI, 2020). These antibiotics included amoxicillin/clavulanic acid, ampicillin/sulbactam, cefazolin, ceftazidime, ceftriaxone, ciprofloxacin, levofloxacin, amikacin, aztreonam, gentamicin, imipenem and meropenem.

Data collection

Data collected from the medical record database included demographic data (age and gender), symptoms and underlying diseases, laboratory and microbiological findings, complications, antimicrobial therapy, necessity of interventional treatment (percutaneous drainage, or surgical drainage) and clinical outcomes (i.e., cured or died).

Statistical analysis

Data entry and processing was conducted using SPSS software, version 20.0 (IBM Inc., New York, USA). Descriptive data were presented as means±SD, categorical variables were reported as number and percentage. The Student's t-test and the Mann-Whitney U test were applied to evaluate continuous variables. We analyzed categorical variables using the chi-square or Fisher's exact test. All p-values of < 0.05 were considered as statistically significant.

Results

Demographic data and comorbidities

During the study period, a total of 135 patients diagnosed as K. pneumoniae liver abscess were included. Demographic characteristics, symptoms and underlying diseases of patients with sepsis (n=37) and patients of the non-sepsis group (n=98) were summarized in Table 1. Eighty (59.3%) were males and fifty-five (40.7%) were females. Mean age at diagnosis of the enrolled patients was 60.9±12.7 years (range 23 to 88). Presences of fever, chills, abdominal pain, were predominant symptoms between two groups. There were significant differences in the following variables in the sepsis group compared to the non-sepsis group: frailty (32.4% vs. 12.2%, p=0.006), diarhea (18.9% vs. 2.0%, p=0.002). However, the sepsis group was less likely to have abdominal pain (10.8% vs. 55.1%, p=0.000). KLPA patients with sepsis had a higher rate of fatty liver (24.3% vs. 7.1%, p=0.006), chronic renal insuficiency (35.1% vs. 1.0%, p=0.000) and hepatic dysfunction (45.9% vs. 4.1%, p=0.000) (Table 1).

Imaging and laboratory results

Laboratory findings recorded on admission are shown in Table 2. According to these images, there were no obviously differences between the two groups. Most of the lesions (n=90, 66.7%) were located in the right lobe and the abscess size ranged from 5 cm to 10cm. Statistically significant differences between patients with and without sepsis were observed in WBC (p=0.015), neutrophil count (p=0.006), platelets (p=0.000), hemoglobin (p=0.026), total bilirubin (p=0.000), blood urea nitrogen (p=0.000), creatinine (p=0.000).

Complications and treatments

The complications of KPLA patients with and without sepsis are presented in Table 3. More-frequent development of severe complications including septic shock (35.1% vs. 1.0%, p=0.000), and acute respiratory distress syndrome (10.8% vs. 0, p=0.005) were found in the sepsis group. Twelve (8.8%) patients had metastatic infections. The incidence of metastatic infection of the lung (24.3% vs. 2.0, p=0.000) and eye (8.1% vs. 0, p=0.019) was significantly higher in sepsis group. The mean hospital stay was 14.5 ± 9.0 days. KPLA patients with sepsis experience a longer hospital stay with 20.7±9.5 days and a higher proportion of ICU admission (29.7% vs. 3.1%, p=0.000). The treatment of KPLA patients included antibiotics alone (5.2%), antibiotics plus percutaneous drainage (90.4%), antibiotic plus surgical drainage (4.4%). However, there was no significant difference between groups. The most frequently used antibiotics were carbapenems, and followed by third generation cephalosporins, fluoroquinolone, Beta-lactamase inhibitors, or combined with metronidazole. Compared to the non-sepsis group, the sepsis group had a signicantly higher frequency of antibiotic therapy with Beta-lactamase inhibitors (48.6% vs. 20.4%, p=0.001) and carbapenems (83.8% vs. 66.3%, p=0.046). However, no significant difference was found in mortality between the two groups.

Antimicrobial susceptibility

Among the 135 patients, only 4 K. pneumoniae strains was ESBL-producing. All the strains were intrinsically resistant to ampicillin, and were unsusceptible to amoxicillin/clavulanic acid, cefazolin, 6 to ampicillin/ sulbactam, levofloxacin, 4 to ceftazidime, ciprofloxacin, aztreonam, gentamicin, 2 to imipenem, meropenem (Table 4). All of these strains were susceptible to amikacin.

Metastatic infection

The characteristics of the 12 patients with metastatic infection are shown in table 5. Among them, 10 had abscesses in the right hepatic lobe, 2 in the left hepatic lobe. The most frequent complications were septic shock and acute respiratory distress syndrome. Metastatic infection involved multiple sites, such
as lung, eye, central nervous system, which was easy to cause serious consequences, especially in patients with endophthalmitis, more disabled; and those involving central nervous system were more critical. Four KPLA patients had endophthalmitis, and one patient had central nervous system infection. Eventually, two patients died from complications.

**Characteristics and outcome of KPLA patients with or without metastatic infections**

Table 6 compares clinical manifestations, laboratory findings and outcome of KPLA patients with or without metastatic infections. There were no differences between two groups in these symptoms and underlying conditions. However, patients with metastatic infections were more likely to suffer chronic renal insufficiency (41.7% vs. 7.3%, \( p=0.000 \)) than these without metastatic infections. There was a statistical difference in platelets \( (p=0.015) \), total bilirubin \( (p=0.049) \), blood urea nitrogen \( (p=0.003) \) and creatinine \( (p=0.006) \), which were higher in the metastatic infections group. In regards to mortality, the metastatic infections group was significantly higher than the non-metastatic infection group \( (p=0.007) \).

**Discussion**

KPLA is a critical infectious disease, which could cause sepsis and/or other severe complications. However, few studies on the complications of KPLA have been published. In this study, KPLA was diagnosed in 135 of the 360 (37.5%) patients, and the incidence of sepsis in KPLA was 27.4% (37 of 135 patients). Our study found the sepsis group was more likely to have the metastatic infections with lung and eye.

A large proportion of the patients in our study were males, with the average age of 60.9±12.7 years old, compared with previous studies\(^{22,15}\). Zhang J et al. reported that elderly patients with age over of 65 years were more likely to develop pyogenic liver abscess\(^{16}\). The previous studies reported that the mean age was 59.6 years, and the age group with the greatest number of patients was 51 to 60 years\(^{17}\). In present study, the results showed that men were more likely to develop sepsis than women. Hormonally active women are better protected from sepsis than men. Sex hormones play an important role in inflammatory responses\(^{18}\). It was notable that fever was present in 91.1% of patients, which was consistent with other studies\(^{19}\). In our study, 50.0% of KPLA patients were diabetic. As reported previously, diabetes mellitus were the most common underlying disease in KPLA patients\(^{20}\). The functional abnormality in neutrophil chemotaxis and phagocytosis may contribute to a relatively high incidence of KPLA in diabetes mellitus. In this investigation, we found that sepsis patients had a higher incidence of frailty, diarrhea, which were non-specific and may lead to a delayed diagnosis of PL. Furthermore, patients with sepsis had a significantly higher prevalence of underlying diseases with fatty liver, chronic renal insufficiency, hepatic dysfunction, which indicates that PLA patients with sepsis had a greater incidence of metabolic disorders.

The laboratory features are also non-specific for the diagnosis of KPLA. Most patients had increased levels of white blood cell counts (WBC), neutrophil percentage (NE%), C-reactive protein (CRP), procalcitonin (PCT), fibrinogen, which were considered to be the markers for infection. Furthermore, blood urea nitrogen and creatinine levels of the sepsis group were higher, which suggests that renal insufficiency in KPLA patients with sepsis was more evident. In addition, these laboratory examinations may reduce the misdiagnosis of PLA.

Extrahepatic metastatic infection is one of the fatal complications for KPLA patients\(^{21}\). Recently, \( K. pneumoniae \) liver abscess with septic metastatic lesions has been often reported\(^{22,23}\). KPLAs were associated with metastatic infection especially including eye or central nervous system (CNS), which is consistent with several studies that metastatic infections are more common in KPLAs than non-KPLAs and the prevalence rate of metastatic infections has increased\(^{24}\). In this investigation, the incidence of extrahepatic metastatic infection in KPLA was 8.8%, which was consistent with previous reports\(^{15,25}\). We observed that KPLA patients with sepsis may be more likely to have some complications, including acute kidney injury, acute respiratory distress syndrome, and spontaneous bacterial peritonitis. The sepsis group also revealed a high incidence of metastatic infection. Our results corresponded to the previous investigations, this may be due to the failure of liquefaction owing to the high prevalence of a phagocytosis-resistant, capsular serotype \( Klebsiella pneumoniae \) associated with liver abscess\(^{26}\). In our study, 12 patients with KPLA had severe metastatic infectious conditions at admission. The mortality was 1.5% overall, and 2 of them died of overwhelming sepsis and multiple organ failure. Our data showed that three patients had endophthalmitis. Despite aggressive intravenous and intravitreal antibiotic therapy, 2 of them were eventually eviscerated or enucleated. Other associated septic metastatic infections included pulmonary infection in 11 cases, pleural effusion in 4 cases, brain abscess or meningitis in 1 case, and peritonitis in 1 case.

In the present study, we found that most of the \( K. pneumoniae \) strains isolated were susceptible to most of the antibiotics, but with resistance only to ampicillin. Previous studies also reported that the emergence of carbapenem-resistant \( K. pneumoniae \) in some strains may lead to final treatment failure. Therefore, the antibiotics are most widely used in current clinical practice. However, the rising trend in resistance have been reported elsewhere in the world. As known the capsule of \( K. pneumoniae \) may play an important role in the resistance of uptake and killing by host phagocytes\(^{27}\), it is prudent to ensure sensitivity-directed antibiotics therapy during KPLA treatment to prevent further development of antibiotic resistance.

In general, strategy of therapeutic methods was dependent on the size and number of abscesses, degree of abscess liquefaction, and with/without other possible complications. In our study, the first treatment was antibiotics and percutaneous pigtail catheter drainage of KPLA, followed by antibiotic alone. Intravenous antibiotics were given to all these patients and 90.4% underwent percutaneous drainage, 4.4% underwent surgical drainage. There were no significant differences between these two groups of patients in treatment of PLA. For antibiotic treatment, the most commonly used antibiotics were carbapenem and third generation cephalosporin combined with or without metronidazole. Except for complicated cases, we recognize that appropriate antibiotic coverage and early adequate percutaneous drainage should be considered as the cornerstones of therapy for KPLA patients. As for KPLA patients with severe infectious symptoms at admission, adequate coverage with empirical antibiotics may be reasonable until culture data are available.

We acknowledge the limitations in our study. Firstly, this was a retrospective, single-center study, and may not be generalizable, as the majority of our patients were Chinese. Secondly, we excluded the patients with liver abscesses demonstrated no growth on either blood or pus cultures, which was probably related to...
the use of empirical antibiotics treatment prior to blood or pus collection. In this study, it was excluded because it was hard to specify the pathogen. Finally, whether there is any epidemiologic evidence of the relationship between \textit{K. pneumoniae} capsular serotyping or plasmid-associated virulent factor and the clinical manifestations remains to be investigated. However, we believe that these results may be generalized to routine clinical practice in Chinese patients with pyogenic liver abscess.

In conclusion, PLA is a relatively common infectious disease, and the incidence rate of sepsis in KPLA is quite high. KPLA patients with and without sepsis had many distinct clinical features. Metabolic disorders, including fatty liver, chronic renal insufficiency and hepatic dysfunction are common underlying conditions in patients with sepsis. Furthermore, KPLA patients with sepsis had a significantly higher risk of severe metastatic complications, including lung and eye infections. Based on our data, it is necessary to further elucidate the clinical and microbiological features of KPLA, with a focus on septic metastatic infection.

\textbf{Abbreviations}

PLA
Pyogenic liver abscess; KPLA: Klebsiella pneumoniae-caused liver abscesses.

\textbf{Declarations}

\textbf{Acknowledgements}

We would like to thank Clinical Microbiology Laboratory for supporting this study.

\textbf{Authors' contributions}

SX L and P Z had roles in the study design, data analysis, literature search, and writing of the manuscript. SF Y and MF P had roles in research guiding, and clinical management. CY X, JJ Q, J Q and MM H had roles in data collection, and data interpretation. All authors have read and agreed with the final manuscript.

\textbf{Funding information}

This work was supported by grants from Taizhou Technology Project, Zhejiang Province (1902ky08).

\textbf{Availability of data and materials}

The datasets analysed during the current study are available from the corresponding author on reasonable request.

\textbf{Ethics approval and consent to participate}

The Institutional Medical Ethics Committee of Taizhou Hospital of Zhejiang Province granted approval for this retrospective study, with a waiver of informed consent because the medical records of the subjects were deidentified from the Medical Records and Statistics Room to ensure patient confidentiality. All study procedures were conducted in accordance with the Declaration of Helsinki. The use of the raw data was permitted by the Institutional Medical Ethics Committee of Taizhou Hospital of Zhejiang Province.

\textbf{Consent for publication}

Not applicable.

\textbf{Competing interests}

The authors declare no competing interests.

\textbf{References}

1. Qian Y, Wong CC, Lai S et al (2016) A retrospective study of pyogenic liver abscess focusing on Klebsiella pneumoniae as a primary pathogen in China from 1994 to 2015. Sci Rep 6:38587.
2. Li WF, Chen HJ, Wu S et al (2018) A comparison of pyogenic liver abscess in patients with or without diabetes: a retrospective study of 246 cases. BMC Gastroenterology 18(1):144.
3. Siu LK, Yeh KM, Lin JC et al (2012) Klebsiella pneumoniae liver abscess: a new invasive syndrome. The Lancet Infectious Diseases 12(11):881-887.
4. Wang HR, Ren Y, Chang ZH et al (2020) The increased recurrence rate of liver abscess caused by extended-spectrum beta-lactamase-producing Klebsiella pneumoniae. Eur J Clin Microbiol Infect Dis 39(7):1315-1320.
5. Hsieh CB, Tzao C, Yu CY et al (2006) APACHE II score and primary liver cancer history had risk of hospital mortality in patients with pyogenic liver abscess. Dig Liver Dis 38(7):498-502.
6. Zhang S, Zhang X, Wu Q et al (2019) Clinical, microbiological, and molecular epidemiological characteristics of -induced pyogenic liver abscess in southeastern China. Antimicrobial resistance infection control 8:166.
7. Buppajartham S, Shah M, Junpaparp P (2014) Tumor-like pyogenic liver abscess caused by Klebsiella pneumoniae in diabetes. Endocrine 47(2):656-657.
8. Cerwenka H(2010) Pyogenic liver abscess: differences in etiology and treatment in Southeast Asia and Central Europe. World journal of gastroenterology 16(20):2458-2462.

9. Lee JH, Jang YR, Ahn SJ et al(2020) A retrospective study of pyogenic liver abscess caused primarily by Klebsiella pneumoniae vs. non-Klebsiella pneumoniae: CT and clinical differentiation. Abdom Radiol (NY) 45(9):2669-2679.

10. Lee SS, Chen YS, Tsai HC et al(2008) Predictors of septic metastatic infection and mortality among patients with Klebsiella pneumoniae liver abscess. Clin Infect Dis 47(5):642-650.

11. Martin GS(2012) Sepsis, severe sepsis and septic shock: changes in incidence, pathogens and outcomes. Expert Rev Anti Infect Ther 10(6):701-706.

12. Cho Hy, Lee ES, Lee YS et al(2017) Predictors of septic shock in initially stable patients with pyogenic liver abscess. Scand J Gastroenterol 52(5):589-594.

13. Seymour CW, Liu VX, Iwashyna TJ et al(2016) Assessment of Clinical Criteria for Sepsis: For the Third International Consensus Definition for Sepsis and Septic Shock (Sepsis-3). JAMA 315(8):762-774.

14. Talan DA, Moran GJ, Abrahamian FM(2008) Severe sepsis and septic shock in the emergency department. Infect Dis Clin North Am 22(1):1-31.

15. Lok KH, Li KF, Li KK et al(2008) Pyogenic liver abscess: clinical profile, microbiological characteristics, and management in a Hong Kong hospital. J Microbiol Immunol Infect 41(6):483-490.

16. Zhang J, Du Z, Bi J et al(2019) Comparison of clinical characteristics and outcomes of pyogenic liver abscess patients < 65 years of age versus ≥ 65 years of age. BMC Infect Dis 19(1):233.

17. Zhu X, Wang S, Jacob R et al(2011) A 10-year retrospective analysis of clinical profiles, laboratory characteristics and management of pyogenic liver abscesses in a Chinese hospital. Gut Liver 5(2):221-227.

18. Kawasaki T, Chaudry IH(2012) The effects of estrogen on various organs: therapeutic approach for sepsis, trauma, and reperfusion injury. Part 2: liver, intestine, spleen, and kidney. J Anesth 26(6):892-899.

19. Qu TT, Zou HC, Jiang Y et al(2015) Clinical and microbiological characteristics of Klebsiella pneumoniae liver abscess in East China. BMC Infect Dis 15:161.

20. Foo NP, Chen KT, Lin HJ et al(2010) Characteristics of Pyogenic Liver Abscess Patients With and Without Diabetes Mellitus. American Journal of Gastroenterology 105(2):328-335.

21. Lin YT, Liu CJ, Chen TJ et al(2012) Long-term mortality of patients with septic ocular or central nervous system complications from pyogenic liver abscess: a population-based study. PLoS One 7(3):e33978.

22. Ohmori S, Shiraki K, Ito K et al(2002) Septic endophthalmitis and meningitis associated with Klebsiella pneumoniae liver abscess. Hepatology Research 22(4):307-312.

23. Gupta A, Bhatti S, Leytin A et al(2018) Novel complication of an emerging disease: Invasive liver abscess syndrome as a cause of acute respiratory distress syndrome. Clin Pract 8(1):1021.

24. Chang FY, Chou MY(1995) Comparison of pyogenic liver abscesses caused by Klebsiella pneumoniae and non-K. pneumoniae pathogens. J Formos Med Assoc 94(5):232-237.

25. Yoon JH, Kim YJ, Jun YH et al(2014) Liver abscess due to Klebsiella pneumoniae: risk factors for metastatic infection. Scand J Infect Dis 46(1):21-26.

26. Lau YJ, Hu BS, Wu WL et al(2000) Identification of a major cluster of Klebsiella pneumoniae isolates from patients with liver abscess in Taiwan. J Clin Microbiol 38(1):412-414.

27. Kohayagawa Y, Nakao K, Ushita M et al(2009) Pyogenic liver abscess caused by Klebsiella pneumoniae genetic serotype K1 in Japan. J Infect Chemother 15(4):248-251.

Tables
| Characteristic                      | Total n = 135 | KPLA with sepsis n = 37 | KPLA without sepsis n = 98 | P value |
|------------------------------------|---------------|-------------------------|-----------------------------|---------|
| Age (year)                         | 60.9 ± 12.7   | 61.1 ± 12.1             | 60.8 ± 13.0                 | 0.902   |
| Gender                             |               |                         |                             | 0.227   |
| Male, n(%)                         | 80(59.3)      | 25(67.6)                | 55(56.1)                    |         |
| Female, n(%)                       | 55(40.7)      | 12(32.4)                | 43(43.9)                    |         |
| Symptoms                           |               |                         |                             |         |
| Body temperature (≥ 38.5°C)        | 80(59.3)      | 21(56.8)                | 59(60.2)                    | 0.716   |
| Fever                              | 123(91.1)     | 35(94.6)                | 88(89.8)                    | 0.511a  |
| Chills                             | 81(60.0)      | 24(64.9)                | 57(58.2)                    | 0.478   |
| Abdominal pain                     | 58(43.0)      | 4(10.8)                 | 54(55.1)                    | 0.000   |
| Nausea                             | 17(12.6)      | 5(13.5)                 | 12(12.2)                    | 0.843   |
| Vomiting                           | 16(11.9)      | 7(18.9)                 | 9(9.2)                      | 0.119   |
| Frailty                            | 24(17.8)      | 12(32.4)                | 12(12.2)                    | 0.006   |
| Diarrhea                           | 9(6.7)        | 7(18.9)                 | 2(2.0)                      | 0.002a  |
| Underlying conditions              |               |                         |                             |         |
| Diabetes mellitus                  | 67(50.0)      | 20(54.1)                | 47(48.0)                    | 0.528   |
| Hypertension                       | 51(37.8)      | 17(45.9)                | 34(34.7)                    | 0.229   |
| Fatty liver                        | 16(11.9)      | 9(24.3)                 | 7(7.1)                      | 0.006   |
| Cholelithiasis                     | 29(21.5)      | 4(10.8)                 | 25(25.5)                    | 0.064   |
| Viral hepatitis                    | 32(23.7)      | 7(18.9)                 | 25(25.5)                    | 0.422   |
| Cardiovascular diseases            | 25(18.5)      | 5(13.5)                 | 20(20.4)                    | 0.358   |
| Chronic renal insufficiency        | 14(10.4)      | 13(35.1)                | 1(1.0)                      | 0.000a  |
| Hepatic dysfunction                | 21(15.6)      | 17(45.9)                | 4(4.1)                      | 0.000a  |
| Abdominal surgery history          | 9(6.7)        | 0                       | 9(9.2)                      | 0.063a  |

*a Calculated with the Fisher's exact test
| Characteristic         | Total n = 135 | KPLA with sepsis n = 37 | KPLA without sepsis n = 98 | P value |
|------------------------|---------------|-------------------------|---------------------------|---------|
| Abscess location       |               |                         |                           |         |
| Right lobe             | 90(66.7)      | 25(67.6)                | 65(66.3)                  | 0.891   |
| Left lobe              | 34(25.2)      | 9(24.3)                 | 25(25.5)                  | 0.887   |
| Both lobes             | 11(8.1)       | 3(8.1)                  | 8(8.2)                    | 1.000a  |
| Abscess size(cm)       |               |                         |                           |         |
| < 5                    | 26(19.3)      | 5(13.5)                 | 21(21.4)                  | 0.298   |
| 5–10                   | 85(63.0)      | 24(64.9)                | 61(62.2)                  | 0.779   |
| > 10                   | 24(17.8)      | 8(21.6)                 | 16(16.3)                  | 0.473   |
| Laboratory findings    |               |                         |                           |         |
| WBC > 9.5×10^9/L       | 105(77.8)     | 34(91.9)                | 71(72.4)                  | 0.015   |
| NE% > 75%              | 119(88.1)     | 37(100.0)               | 82(83.7)                  | 0.006a  |
| PLT < 125×10^9/L       | 38(28.1)      | 19(51.4)                | 19(19.4)                  | 0.000   |
| Hb < 110 g/L           | 37(27.4)      | 5(13.5)                 | 32(32.7)                  | 0.026   |
| CRP > 10mg/L           | 127(94.1)     | 37(100.0)               | 90(91.8)                  | 0.106a  |
| PCT > 0.5ng/ml         | 120(88.9)     | 35(94.6)                | 85(86.7)                  | 0.237a  |
| ALT > 50U/L            | 73(54.1)      | 23(62.2)                | 50(51.0)                  | 0.247   |
| AST > 40U/L            | 79(58.5)      | 25(67.6)                | 54(55.1)                  | 0.190   |
| ALP > 125U/L           | 100(74.1)     | 26(70.3)                | 74(75.5)                  | 0.535   |
| GGT > 60U/L            | 105(77.8)     | 30(81.1)                | 75(76.5)                  | 0.571   |
| T.Bil > 20.5µmol/L     | 44(32.6)      | 22(59.5)                | 22(22.7)                  | 0.000   |
| ALB < 40 g/L           | 129(95.6)     | 37(100.0)               | 92(93.9)                  | 0.188a  |
| FIB > 4g/L             | 128(94.8)     | 33(89.2)                | 95(96.9)                  | 0.089a  |
| APTT > 42s             | 80(59.3)      | 20(54.1)                | 60(61.2)                  | 0.449   |
| BUN > 7.2 mmol/L       | 41(30.4)      | 21(56.8)                | 19(19.6)                  | 0.000   |
| Cr > 97µmol/L          | 20(14.8)      | 12(32.4)                | 8(8.2)                    | 0.000   |

WBC white blood cell count, NE% neutrophil percentage, PLT platelets, Hb hemoglobin, CRP C-reactive protein, PCT procalcitonin, ALT Alanine Transaminase, AST Aspartate Transaminase, ALP Alkaline Phosphatase, GGT Gamma-Glutamyl Transpeptidase, T.BIL Total bilirubin, ALB Albumin, FIB Fibrinogen, APTT Activated Partial Thromboplastin Time, BUN blood urea nitrogen, Cr creatinine
Table 3
Treatment, complications and outcomes of patients with *K. pneumoniae* liver abscess with sepsis or without sepsis

| Characteristic                          | Total n = 135 | KPLA with sepsis n = 37 | KPLA without sepsis n = 98 | P value  |
|----------------------------------------|---------------|-------------------------|----------------------------|----------|
| Complications                          |               |                         |                            |          |
| Sepsis shock                           | 8(5.9)        | 7(18.9)                 | 1(1.0)                     | 0.000*    |
| Acute Respiratory Distress Syndrome    | 4(3.0)        | 4(10.8)                 | 0                          | 0.005*    |
| Acute kidney injury                    | 2(1.5)        | 2(5.4)                  | 0                          | 0.074*    |
| Pleural effusion                       | 11(8.1)       | 4(10.8)                 | 7(7.1)                     | 0.493*    |
| Spontaneous bacterial peritonitis      | 2(1.5)        | 2(5.4)                  | 0                          | 0.074*    |
| Metastatic infections                  |               |                         |                            |          |
| Lung                                   | 11(8.1)       | 9(24.3)                 | 2(2.0)                     | 0.000*    |
| Eye                                    | 4(3.0)        | 4(10.8)                 | 0                          | 0.005*    |
| CNS                                    | 1(0.7)        | 1(2.7)                  | 0                          | 0.274*    |
| Others                                 | 4(3.4)        | 3(8.1)                  | 1(1.0)                     | 0.063*    |
| Hospital length of stay, days          | 14.5 ± 9.0    | 20.7 ± 9.5              | 12.2 ± 7.7                 | 0.000     |
| ICU admission                          | 14(10.4)      | 11(29.7)                | 3(3.1)                     | 0.000*    |
| Readmission                            | 8(5.9)        | 2(5.4)                  | 6(6.1)                     | 1.000*    |
| Treatment                              |               |                         |                            | 0.696     |
| Antibiotics alone                      | 7(5.2)        | 1(2.7)                  | 6(6.1)                     |           |
| Antibiotics + Percutaneous drainage    | 122(90.4)     | 34(91.9)                | 88(89.8)                   |           |
| Antibiotics + Surgical drainage        | 6(4.4)        | 2(5.4)                  | 4(4.1)                     |           |
| Antibiotic drugs                       |               |                         |                            |           |
| Beta-lactamase inhibitors              | 38(28.1)      | 18(48.6)                | 20(20.4)                   | 0.001     |
| The third generation of cephalosporin  | 59(43.7)      | 18(48.6)                | 41(41.8)                   | 0.477     |
| Fluoroquinolone                        | 51(37.8)      | 17(45.9)                | 34(34.7)                   | 0.229     |
| Carbapenems                            | 96(71.1)      | 31(83.8)                | 65(66.3)                   | 0.046     |
| Metronidazole                          | 57(42.2)      | 16(43.2)                | 41(41.8)                   | 0.883     |
| Clinical outcomes                      |               |                         |                            | 0.074*    |
| Cured                                  | 133(98.5)     | 35(94.6)                | 98(100)                    |           |
| Died (Poor prognosis)                  | 2(1.5)        | 2(5.4)                  | 0                          |           |

Table 4
Antibiotics resistance among *K. pneumoniae* isolates

| No. of isolates | Amoxicillin/clavulanic acid | Ampicillin/sulbactam | Cefazolin | Ceftazidime | Ceftriaxone | Ciprofloxacin | Levofloxacin | Amikacin | Aztreonam | Imipenem |
|----------------|----------------------------|----------------------|-----------|-------------|-------------|---------------|--------------|-----------|-----------|----------|
| 2              | R                          | R                    | R         | R           | R           | R             | S            | R         | R         | R        |
| 2              | R                          | R                    | R         | R           | R           | R             | S            | R         | R         | S        |
| 2              | R                          | R                    | S         | S           | R           | S             | S            | S         | S         | S        |
| 2              | R                          | S                    | R         | S           | S           | S             | S            | S         | S         | S        |
| 127            | S                          | S                    | S         | S           | S           | S             | S            | S         | S         | S        |
| Patient | Age, years | Sex | Infection site | Underlying disease(s) | Severe complication(s) | Location of abscess | WBC (X10^9/L) | Neutrophil (%) | CRP (mg/L) | PCT (ng/ml) | Anti-hist | Antibiotics |
|---------|------------|-----|----------------|------------------------|------------------------|---------------------|---------------|----------------|-------------|-------------|-----------|-------------|
| 1       | 60         | F   | Lung           | HTN, chronic renal insufficiency | MODF, ARDS, AKI, Septic shock | Left side | 12.7 | 88 | 136 | 76 | IMP |
| 2       | 55         | M   | Lung peritoneum| DM                     | Septic shock          | Right side | 12.6 | 92 | 316 | 157.7 | MEM, MXF |
| 3       | 58         | M   | Lung eye       | None                    | None                  | Right side | 14.2 | 81 | 74.1 | 0.49 | CRO |
| 4       | 46         | M   | Lung eye       | HTN, DM, liver cirrhosis| Septic shock          | Right side | 10 | 87.7 | 137.8 | 7.77 | IMP, MXF |
| 5       | 82         | F   | Lung pleura    | HTN, Cholelithiasis, Cardiovascular diseases | None | Right side, multiple | 15.6 | 88 | 104 | 1.55 | MXF, MEM |
| 6       | 50         | F   | Lung           | chronic hepatitis      | MODF, ARDS, Septic shock, DIC | Right side | 21.5 | 96.3 | 176.7 | 100 | CAZ, MEM, LEV |
| 7       | 32         | M   | Lung           | HTN, DM,               | Septic shock, ARDS    | Right side | 11.4 | 89.6 | 238.6 | 8.49 | IMP, MXF |
| 8       | 83         | F   | Lung           | Cardiovascular diseases | Septic shock          | Right side, multiple | 10.6 | 93.3 | 311.18 | 73 | CRO |
| 9       | 61         | M   | Lung CNS eye   | HTN, DM, Cardiovascular diseases | ARDS | Right side, multiple | 23.4 | 95.5 | 113.1 | 24.2 | CRO, MEM |
| 10      | 48         | M   | Lung eye       | HTN, DM,               | None                  | Right side | 33.3 | 89.5 | 132.5 | 20.32 | TZP |
| 11      | 53         | F   | Lung pleura    | HTN, DM, anemia        | AKI                   | Right side | 9.3 | 94.2 | 267.9 | 23.25 | TZP, CAZ |
| 12      | 53         | F   | Pleura         | DM, anemia             | None                  | Left side | 10.4 | 82.5 | 130.8 | 25.8 | TZP |

HTN hypertension; MODF multiple organ dysfunction syndrome; ARDS acute respiratory distress syndrome; DIC disseminated intravascular coagulation; AKI Acute Kidney Injury; TZP Piperacillin/tazobactam, LEV Levofloxacin, IMP Imipenem, MEM Meropenem, CAZ Ceftazidime, CRO ceftriaxone, MXF Moxifloxacin, SCF Cefperazone/t
Table 6
Baseline characteristics, clinical presentation, and outcome of patients with *K. pneumoniae* liver abscess with or without metastatic infections

| Characteristic                          | Total n = 135 | KPLA with Metastatic infection n = 12 | KPLA without Metastatic infection n = 123 | P value |
|----------------------------------------|---------------|--------------------------------------|------------------------------------------|---------|
| Age (year)                             | 60.9 ± 12.7   | 58.3 ± 12.2                          | 61.1 ± 12.8                              | 0.467   |
| Gender                                 |               |                                      |                                          | 0.494   |
| Male,n(%)                              | 80 (59.3)     | 6 (50.0)                             | 74 (60.2)                                |         |
| Female,n(%)                            | 55 (40.7)     | 6 (50.0)                             | 49 (39.8)                                |         |
| Symptoms                               |               |                                      |                                          |         |
| Body temperature (≥ 38.5°C)            | 80 (59.3)     | 7 (58.3)                             | 73 (59.3)                                | 0.945   |
| Fever                                  | 123 (91.1)    | 11 (91.7)                            | 112 (91.1)                               | 1.000<sup>a</sup> |
| Chills                                 | 81 (60.0)     | 8 (66.7)                             | 73 (59.3)                                | 0.621   |
| Abdominal pain                         | 58 (43.0)     | 6 (50.0)                             | 52 (42.3)                                | 0.606   |
| Nausea                                 | 17 (12.6)     | 2 (16.7)                             | 15 (12.2)                                | 0.648<sup>a</sup> |
| Vomiting                               | 16 (11.9)     | 2 (16.7)                             | 14 (11.4)                                | 0.635<sup>a</sup> |
| Frailty                                | 24 (17.8)     | 2 (16.7)                             | 22 (17.9)                                | 1.000<sup>a</sup> |
| Diarrhea                               | 9 (6.7)       | 0                                    | 9 (7.3)                                  | 1.000<sup>a</sup> |
| Underlying conditions                  |               |                                      |                                          |         |
| Diabetes mellitus                      | 67 (50.0)     | 7 (58.3)                             | 60 (48.8)                                | 0.528   |
| Hypertension                           | 51 (37.8)     | 6 (50.0)                             | 45 (36.6)                                | 0.360   |
| Fatty liver                            | 16 (11.9)     | 1 (8.3)                              | 15 (12.2)                                | 1.000<sup>a</sup> |
| Cholelithiasis                         | 29 (21.5)     | 1 (8.3)                              | 28 (22.8)                                | 0.461<sup>a</sup> |
| Viral hepatitis                        | 32 (23.7)     | 2 (16.7)                             | 30 (24.4)                                | 0.731<sup>a</sup> |
| Cardiovascular diseases                | 25 (18.5)     | 3 (25.0)                             | 22 (17.9)                                | 0.696<sup>a</sup> |
| Chronic renal insufficiency           | 14 (10.4)     | 5 (41.7)                             | 9 (7.3)                                  | 0.000   |
| Hepatic dysfunction                    | 21 (15.6)     | 3 (25.0)                             | 18 (14.6)                                | 0.399<sup>a</sup> |
| Abdominal surgery history             | 9 (6.7)       | 1 (8.3)                              | 8 (6.5)                                  | 0.579<sup>a</sup> |
| Abscess location                       |               |                                      |                                          |         |
| Right lobe                            | 90 (66.7)     | 10 (83.3)                            | 80 (65.0)                                | 0.199   |
| Left lobe                             | 34 (25.2)     | 2 (16.7)                             | 32 (26.0)                                | 0.730<sup>a</sup> |
| Both lobes                            | 11 (8.1)      | 0                                    | 11 (8.9)                                 | 0.598<sup>a</sup> |
| Laboratory findings                   |               |                                      |                                          |         |
| WBC > 9.5× 10<sup>9</sup>/L            | 105 (77.8)    | 10 (83.3)                            | 95 (77.2)                                | 0.628   |
| NE% > 75%                              | 119 (88.1)    | 12 (100.0)                           | 107 (87.0)                               | 0.359<sup>a</sup> |
| PLT < 125                              | 38 (28.1)     | 7 (58.3)                             | 31 (25.2)                                | 0.015   |
| Hb < 110 g/L                           | 37 (27.4)     | 2 (16.7)                             | 35 (28.5)                                | 0.511<sup>a</sup> |
| CRP > 10mg/L                           | 127 (94.1)    | 12 (100.0)                           | 105 (85.4)                               | 0.367<sup>a</sup> |
| PCT > 0.5ng/ml                         | 120 (88.9)    | 12 (100.0)                           | 108 (87.8)                               | 0.360<sup>a</sup> |
| ALT > 50U/L                            | 73 (54.1)     | 5 (41.7)                             | 68 (55.3)                                | 0.366   |
| AST > 40U/L                            | 79 (58.5)     | 7 (58.3)                             | 72 (58.5)                                | 0.989   |
| ALP > 125U/L                           | 100 (74.1)    | 10 (83.3)                            | 90 (73.2)                                | 0.443   |
| Characteristic       | Total          | KPLA with Metastatic infection | KPLA without Metastatic infection | P value |
|---------------------|----------------|-------------------------------|----------------------------------|---------|
|                     | n = 135        | n = 12                        | n = 123                          |         |
| GGT > 60U/L         | 105(77.8)      | 8 (66.7)                      | 97 (78.9)                        | 0.332   |
| T.Bil > 20.5µmol/L  | 44 (32.6)      | 7 (58.3)                      | 37 (30.3)                        | 0.049   |
| ALB < 40 g/L        | 129 (95.6)     | 12 (100.0)                    | 117 (95.1)                       | 1.000a  |
| FIB > 4g/L          | 128 (94.8)     | 11 (91.7)                     | 117 (95.1)                       | 0.487a  |
| APTT > 42s          | 80 (59.3)      | 6 (50.0)                      | 74 (60.2)                        | 0.494   |
| BUN > 7.2 mmol/L    | 41 (30.4)      | 8 (66.7)                      | 32 (26.2)                        | 0.003   |
| Cr > 97µmol/L       | 20 (14.8)      | 5 (41.7)                      | 15 (12.3)                        | 0.006   |
| Treatment           |                |                               |                                  | 0.075   |
| Antibiotics alone   | 7 (5.2)        | 0                             | 7 (5.7)                          |         |
| Antibiotics + Percutaneous drainage | 122 (90.4) | 10 (83.3)                      | 112 (91.1)                       |         |
| Antibiotics + Surgical drainage | 6 (4.4) | 2 (16.7)                      | 4 (3.3)                          |         |
| Clinical outcomes   |                |                               |                                  | 0.007a  |
| Cured               | 133 (98.5)     | 10 (83.3)                     | 123 (100.0)                      |         |
| Poor prognosis      | 2 (1.5)        | 2 (16.7)                      | 0                                |         |