

Management of 96 Patients with Pyogenic Liver Abscess Admitted to a Single Hospital in Hanoi City, Vietnam, 2015-2020: Etiology, Drug Resistance, Complications, and the Outcomes

Cong Long Nguyen^{1,2}, Truong Khanh Vu^{1,2}, Van Son Tran³, Nghe Tinh Nguyen¹, Thi Van Ngoc Pham¹, Thi Binh An Nguyen⁴, Doan Long Dinh² and Ngoan Tran Le^{5,6*}



¹Gastroenterology and Hepatology Center, Bach Mai Hospital, Vietnam

²University of Medicine and Pharmacy, Vietnam National University, Vietnam

³Department of Gastroenterology and Hematology Bac Ninh Hospital, Vietnam

⁴Faculty of Health Science, Thang Long University, Vietnam

⁵Institute of Research and Development, Duy Tan University, Viet Nam

⁶Department of Public Health, School of Medicine, International University of Health and Welfare, Japan

*Corresponding author: Ngoan Tran Le, Department of Public Health, School of Medicine, International University of Health and Welfare, Japan

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Abbreviations: PLA: Pyogenic Liver Abscess; ALA: Amoebic Liver Abscess; US: Abdominal Ultrasound; CT: Computed Tomography; MRI: Magnetic Resonance Image; AST: Aspartate Aminotransferase; ALT: Alanine Transaminases

ABSTRACT

Objectives: Pyogenic liver abscess (PLA) is an important neglected global health threat during the COVID-19 pandemic and emerged non-communicable diseases. This study aims to investigate the causality and anti-biotic resistance in patients with PLA in Vietnam.

Methods: Clinical features and treatment outcomes of 96 patients with PLA in Bach Mai Hospital from January 2015 to December 2020 were examined. The laboratory and radiological features, microbiological isolates in blood and pus cultures, antibiotics, and the interpretation of the drug sensitivity tests were performed. Demographic and clinical characteristics, treatment outcomes, and management of these patients were evaluated.

Results: All 96 cases were PLA when they were admitted to the hospital and there were 76 (79.2%) cases with positive bacterial results in pus. The common pathogen was *Klebsiella pneumoniae* (56.3%), followed by *Escherichia coli* (7.3%). The isolated *Klebsiella pneumoniae* strains were susceptible to most of the common antibiotics that were used at the clinic, with low rates of resistance (< 10%) except for ampicillin. The proportion of pleural effusion complications among these patients was 44.8%. Ultrasound-guided needle aspiration of PLA was performed in 36 patients (37.5%) and percutaneous abscess drainage was done in 60 patients (62.5%). There were diabetics (31.1%), followed by biliary diseases (13.5%). Antibiotic treatment and percutaneous drainage were the mainstay of management for PLA patients and successfully cured 95 of 96 participants.

Conclusion: Because all patients were admitted to the hospital with serious complications of PLA, *Klebsiella pneumoniae* is sensitive to the most available antibiotics, liver inflammation related to this bacteria would be concerned at the early stage for better treatment outcomes. The longer hospital stay of patients in our study might be explained by the large abscess due to the advanced stage of the disease or neglected liver infectious inflammation.

Introduction

A pyogenic liver abscess (PLA), a suppurating infection of the hepatic parenchyma is associated with high mortality [1,2]. The incidence of PLA is increasing annually but varies worldwide. In Taiwan, according to a retrospective study, the annual incidence of PLA increased gradually from 10.83 to 15.45 cases per 100,000 people from 2000 to 2011 [3]. In the United States, results from a large study indicated that the incidence of PLA was 3.59 cases per 100,000 people and the annual average percent increased 4.1% from 1994 to 2005 [2]. Data from studies in Canada and Denmark showed that the incidences rate of PLA ranged from 1.1 to 2.3 per 100,000 population [4,5]. Many studies is focusing on the prevalence, clinical characteristics, pathogenesis, and bacteriology, as well as management of PLA patients in other countries [1,6]. In Vietnam, only a few studies in the last decades showed that the prevalence of amoebic liver abscess (ALA) was high as much as 21 per 100,000 inhabitants per year [7] but there was a lack of data about the PLA due to another pathogen in Vietnam. Especially, evidence about the clinical characteristics and treatment outcomes in Vietnam has not been reported. Only one study reported the complications of the PLA case [8]. We analyzed etiology by bacteria culture, antibiotics sensitivity as well as the clinical characteristics and treatment outcomes of PLA patients admitted to the Bach Mai University hospital in Vietnam from January 2015 to December 2020.

Methods

Design of Study

A retrospective study was carried out on 96 PLA patients admitted to Bach Mai University hospital, the biggest national hospital in Northern Vietnam, between January 2015 to December 2020. The research protocol was approved by Bach Mai Ethics Committee having a code BM-2015-141 on Sep. 30, 2015.

Inclusions and Exclusions Criteria

The inclusion criteria included patients who were definitively diagnosed with PLA based on clinical findings, abdominal ultrasound (US), microbiology on blood or aspirate culture results. The exclusion criteria included patients aged under 18 years old, amoebic liver abscess, hydatid liver abscess, previous episodes of PLA.

Data Collection

The data were extracted from the medical records: ID, age; sex; main disease and contribute health events; initial symptoms; clinical manifestations; laboratory data; number, size, and location of lesions; microbiological findings by culture and their antibiotic sensitive; diagnostic and treatment methods; treatment

response and mortality. We defined a cryptogenic abscess as a PLA when the obvious source of infection was not found, even though the results of imaging methods and the infection were found. Radiological findings here included abdominal ultrasound, computed tomography (CT), and magnetic resonance image (MRI). A total of 96 etiological samples isolated from the pyogenic liver abscess of the patients was retrospectively analyzed to test the drug sensitivity. The pus culture and drug sensitivity test were performed to identify the pathogens that caused the liver abscess. Pus was directly inoculated on blood agar and MAC agar. Bacteria were identified using the MALDI-TOF system (Bruker, German). The drug sensitivity of the bacteria was determined by analyzing the minimum inhibitory concentration using the M50 system (Phoenix, USA). Cultures were isolated for aerobic and anaerobic organisms using the standard diagnostic techniques.

If both blood and pus cultures were positive, bacteria were considered as the etiologic. The selection of antibiotics and the interpretation of the drug sensitivity results were based on American Clinical and Laboratory Standards Institute recommendations [9,10]. The type, duration, and drug administration of all patients who received antibiotics were recorded for each case. Antibiotics were changed based on the results of cultures. If patients still had persistent signs of sepsis after 5 days of intravenous antibiotics, ultrasound-guided percutaneous needle aspiration and drainage were performed. Recovery from PLA was defined as the absence of signs and symptoms together with results of the image. Death from PLA in this study was defined as death during hospitalization and related to PLA.

Data Analysis

Data were presented as mean (range) for numerical values and frequency (percentages) for categorical variables. Statistical analysis was performed using SPSS software (version 23.0, IBM SPSS Statistics, Armonk, NY, USA).

Results

Clinical Characteristics of the Patients

A total of 96 PLA patients, 64 male, and 32 female with a mean age of 53.3±16 years. The most common clinical symptoms were fever 90(93.8%), right upper abdominal pain 92(95.8%), vomiting and nausea in 34(35.4%); Hepatomegaly was reported in 40 cases (41.7%), while right pleural effusion in 43 patients (44.8%) and jaundice in 25 cases (26%) There was a total of 30 patients (31.3%) with diabetes mellitus.

Laboratory and Radiological Features

The common laboratory abnormalities were high white blood cell count (81 cases; 84.4%), the C-reactive protein (92 cases;

95.8%). and procalcitonine (95 cases; 99%) (Table 1). Abdominal ultrasound was implemented in all cases and CT scan and/or MRI were performed in the further diagnosis were needed. The mean size of the liver abscess was 8.5 ± 2.1 cm (min-max: 3.4 – 14.8). There were 80 patients (83.3%) having one abscess when admitted to the hospital. Multiple abscesses were found in 16 cases (16.7%). The presence of gas in the abscess cavity was noted in 12.5% of cases. The abscesses in the right lobe, the left lobe, or in both lobes of the liver were found in 81 patients (84.4%), 10 patients (10.4%), and in 5 patients (5.2%), respectively.

Table 1: Clinical findings and laboratory results for patients with pyogenic liver abscess on presentation.

Characteristic	Values	No. of cases outside the range (%)
Sex (Male/Female)	64/32	
Age (years)	53.3 ± 16	
Underlying conditions		
Biliary diseases	13(13.5)	
Diabetes	30(31.3)	
History of intra-abdominal surgery	2(2.1)	
Fever	90(93.8)	
Right upper abdominal pain	92(95.8)	
Vomiting and nausea	34(35.4)	
Loss of weight	34(35.4)	
Jaundice	25(26)	
Right pleural effusion	43(44.8)	
Ascites	18(18.8)	
Splenomegaly	7(7.3)	
Hepatomegaly	40(41.7)	
AST, U/L	67.9 ± 72.2 (10.0-325.0)	
ALT, U/L	82.1 ± 89.2 (10.0-364.0)	
Bilirubin, mg/dL	27.9 ± 43.8 (4.6-236.5)	
White cell count ($\times 10^3$ /L)	15.8 ± 6.4 (6.1-33.1)	81(84.4)
C-reactive protein, mg/L	53.7 ± 97.2 (0.4-343.8)	92(95.8)
Procalcitonine, ng/mL	8.8 ± 20.2 (0.08-105.0)	95(99)

Note: Values are n (%) or mean \pm standard deviation (SD) unless otherwise specified.

Microbiology and Pathogenesis

The positive results of culture from an aspirate of liver abscess were found in 76 cases (79.2%). The most common pathogen was *Klebsiella pneumoniae* (56.3%), followed by *Escherichia coli* (*E.coli*) (7.3%). Others bacteria were *Klebsiella terrigena* (4.2%),

Streptococcus intermedius (3.1%), *Burkholderia pseudomallei* (2.1%), *Serratia marcescens* (2.1%). The most common underlying disease was diabetics (31.1%), followed by biliary diseases (13.5%).

Management

Patients were treated by image-guided aspiration or drainage of abscess and all patients received intravenous antibiotics before any interventional treatment. Percutaneous aspiration or drainage interventions were performed in different sizes of abscesses. Empirical antibiotic treatment was started at the onset of the clinical infection and changed upon the results of antibiotic susceptibility tests. Ultrasound-guided needle aspiration of PLA was performed in 60 patients (62.5%) and percutaneous abscess drainage was performed in 36 patients (37.5%). The removal of the percutaneous drain was based on the patient's clinical and laboratory response. The median drainage duration was 9.5 ± 6.5 days. The average mean hospital stay was 17.4 ± 7.4 days.

Complications and Outcomes

The systemic effects of the sepsis were in three patients and only one 84 year- old female patient died from severe sepsis due to *Aeromonas hydrophila* after 19 days of treatment.

Results of Analysis of Pathogens

These results indicate that the most common organism identified from the liver abscess aspiration cultures was *Klebsiella pneumoniae*. There were 78 patients (95.1%) who used antibiotics that matched with the sensibility of the bacteria. The empirical treatment was proved to be adequate in most patients. The isolated *Klebsiella pneumoniae* strains were susceptible to most of the common antibiotics that were used at the clinic, with low rates of resistance (< 10%) except for ampicillin (Figure 1). There was 99% of 96 patients recovered after the treated course at the hospital.

Discussion

The most important new findings included the pathogen of *Klebsiella pneumoniae* infection among a large proportion of people suffering from diabetes mellitus and biliary tract diseases. The proportion of pleural effusion complications was nearly half of participating patients. Most available antibiotics could be successfully used to treat the infection from *Klebsiella pneumoniae* in combination with image-guided aspiration or drainage of the abscess. The longer hospital stay of patients in our study might be explained by the large abscess due to the advanced stage of the disease that suggested liver infectious inflammation might be neglected health treats among people having chronic health events of diabetes and biliary tract diseases. Routine screening for liver inflammation due to *Klebsiella pneumoniae* infection and other pathogens including cancer at the early stage for further successful treatment would be recommended.

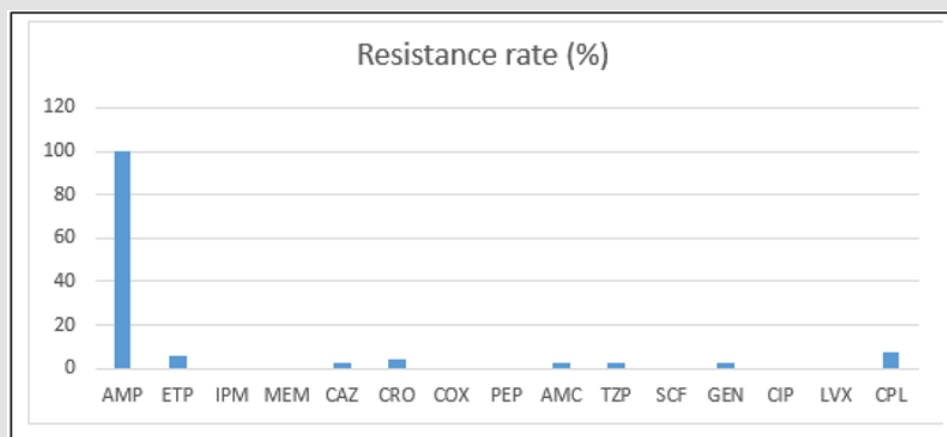


Figure 1: The drug resistance of strains of *Klebsiella pneumoniae*.

Note: AMP= ampicillin, CAZ= ceftazidime, CIP= ciprofloxacin, CRO= ceftriaxone, ETP= ertapenem, GEN= gentamicin, IPM= imipenem, LVX= levofloxacin, MEM= meropenem, TZP= piperacillin/tazobactam, PEP = Cefepime, SCF= Cefoprrazol+Sulbactam, COX= Cefotaxim, AMC= Amoxicillin+ A.clavulanic, CPL= Chloramphenicol.

In this study, the clinical characteristics and treatment outcomes of 96 patients with PLA were reported. The average age of PLA patients in this study was 53.3 years old, lower than the average age of patients with PLA in other studies in the literature (59.1-65 years) [6,11-14]. The common clinical abdominal findings were fever and right upper abdominal pain which were similar to the findings from previous studies [15-18]. However, the proportion of pleural effusion in this study (44.8%) was higher than in the previous study (26.1%-34.5%) [19,20]. The etiologies of PLA have shifted from intra-abdominal infections such as acute appendicitis and trauma to pathologic conditions of the biliary tract; however, up to 55% of patients with PLA have no clear risk factors and these cases are called cryptogenic [21,22]. According to literature, diabetes mellitus is known as an important risk factor of PLA, but the incidences of diabetes mellitus in KP-PLA are varied in different countries, for instance, 38.1% in China [23] and 25% in the United States [24].

Our study also realized that PLA appeared more frequently in patients with diabetes mellitus (31,3%) and biliary tract diseases (13,5%). The position of abscesses was mostly found in the right lobe of the liver and this result was similar to the result of another study [20]. The percentage of cases with the presence of gas within the abscess in our results was 12.5%. Gas-forming in PLA (GFPLA) remains one of the most dangerous complications with a high fatality rate. *Klebsiella pneumoniae* is the most common pathogen causing GFPLA and Gas-forming pyogenic liver abscess, which accounts for 7 to 24% of pyogenic liver abscesses [25]. The results suggested that *K. pneumonia* was the most common microorganism isolated from PLA patients, accounting for 54 cases (56.3%). This result is consistent with recent findings reported in other Asian countries [16,26]. Another study in Europe found that the common

ones were *E. coli* and *Enterococcus* [18,27] but in our study, *E. coli* was the second pathogen causing PLA. In addition, *Klebsiella terrigena*, *Streptococcus intermedius*, *Serratia marcescens*, and *Serratia marcescens* were also pathogens of PLA.

It has been reported that the mortality rate of non-*K. pneumoniae* liver abscess was higher than that of *K. pneumoniae* [28,29]. However, in this study, there was only one death due to *Aeromonas hydrophila* and this finding is similar to the result from another study showing that the mortality rate of PLA has decreased over the years [1]. Septicemia was found in 14 cases (14.6%) in our study. In a previous study in Europe, from 1992 to 2005, mortality associated with PLA was higher, 19% and the main risk factors were the development of sepsis and/or septic shock [20]. According to literature, percutaneous catheter drainage (PCD) was reported more effective than percutaneous needle aspiration (PNA), for example, a study conducted in 306 patients comparing the effectiveness of PCD and PNA in the management of liver abscess showed that PCD was more effective than PNA because of its higher success rate, reducing the time to achieve clinical relief, and supporting a 50% reduction in abscess cavity size [30]. In this study, all patients received antibiotic treatment and underwent percutaneous aspiration or drainage and ultrasound-guided catheter drainage was performed in PLA cases with abscess sizes over 5 cm in diameter.

The overall mean hospital stay was 17.4 ± 7.4 days. The longer hospital stay of patients in our study might be explained by the large abscess due to the advanced stage of the disease, the average size of the abscess among cases was 8.5 cm and the largest size was 14.8 cm. While a retrospective study of PLA focusing on *Klebsiella pneumoniae* in China, Yun Qian, et al. [6] showed that the average

size of the abscess was 6.9 cm and the average length of stay was 18.6 ± 12.9 days. There are some limitations to our study. Firstly, the study was conducted in a hospital that might not be represented the disease in the general population. We only implemented a profile of the antibiotic resistance of *K. pneumoniae*, dominating pathogenic bacteria in PLA. Another limitation is the absence of hepatitis B infection and its role in developing PLA in the present study. Despite some limitations, the study has added new findings of PLD management and treatment, especially in the present study population that would be applied in Vietnam and low-medium developing countries.

The results show that fever and right upper abdominal pain were common initial clinical symptoms among PLA cases. The most common pathogen was *Klebsiella pneumoniae*. The antibiotic treatment and percutaneous drainage were the mainstay of management for PLA patients. This study might provide a valuable reference for clinicians in Vietnam who encounter this uncommon condition. About 20% of PLA has not detected bacteria listed in Table 2 that warrants further significant examination of this disease.

Table 2: Microbiological isolates in blood and pus cultures.

Organism	Pus culture 96 patients n(%)	Blood culture 77 patients n(%)
<i>Klebsiella pneumoniae</i>	54(56.3)	8(10.4)
<i>Escherichia coli</i>	7(7.3)	0
<i>Aeromonas hydrophila</i>	1(1)	1(1.3)
<i>Burkholderia pseudomallei</i>	2(2.1)	1(1.3)
<i>Serratia marcescens</i>	2(2.1)	1(1.3)
<i>Klebsiella terrigena</i>	4(4.2)	1(1.3)
<i>Alcaligenes xylosoxidans</i>	0 (0)	1(1.3)
<i>Staphylococcus aureus</i>	1(1)	0 (0)
<i>Streptococcus intermedius</i>	3(3.1)	0(0)
<i>Streptococcus constellatus</i>	1(1)	
<i>Streptococcus bovis II</i>	1(1)	

Data Availability

Data are included within the manuscript.

Ethical Approval

Ethics approval of this study was given by the Research Ethics Committees of Bach Mai hospital having a code BM-2015-141 on Sep. 30, 2015.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

Funding Statement

School of Medicine and Pharmacy, Vietnam National University Hanoi, Hanoi, Viet Nam, No. QGSP.2021.07.

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Ngoan Tran Le. Biomed J Sci & Tech Res



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