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ORIGINAL ARTICLE

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한국의 고령 화농성 간농양 환자들의 임상적 특성과 예후

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Clinical Characteristics and Outcomes of Pyogenic Liver Abscess in Elderly Korean Patients

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Background/Aims: Incidence of pyogenic liver abscess (PLA) has been increasing worldwide, especially in the elderly population. Therefore, the aim of this study is to elucidate the clinical features and outcomes of PLA in elderly patients.
Methods: A total of 602 patients diagnosed with PLA from January 2003 to January 2013 were analyzed retrospectively. The patients were divided according to two age groups; ≥65 years (n=296) and <65 years (n=306).
Results: The mean age was 73.59±5.98 (range, 65-93) years in the elderly group. Significantly higher incidence of females (52.4% *vs.* 29.1%, p<0.001), hepatobiliary disease (41.2% *vs.* 24.8%, p<0.001), hepatobiliary procedure (29.4% *vs.* 13.7%, p<0.001), underlying malignancy (18.2% *vs.* 4.6%, p<0.001), culture positivity of resistant organism (20.6% *vs.* 14.4%, p=0.047), occurrence of complication (19.6% *vs.* 12.8%, p=0.026), and higher white blood cell (13.44±6.56 *vs.* 12.26±5.89, p=0.021), but lower rates of right lobe abscess (67.2% *vs.* 80.4%, p<0.001), fever (68.6% *vs.* 79.3%, p=0.003), and lower CRP (16.79±9.67 *vs.* 18.80±9.86, p=0.012) was observed in elderly PLA patients, compared to younger patients. Regarding complications, elderly patients had higher incidence of septic shock (8.1% *vs.* 2.3%, p=0.001) and cardiovascular disease (2% *vs.* 0%, p=0.014).
Conclusions: More atypical presentations and complications tend to occur in elderly PLA patients compared with younger patients. Clinicians should be aware of these age-related differences in PLA and devise management strategies accordingly. **(Korean J Gastroenterol 2015;66:27-32)**

Key Words: Pyogenic liver abscess; Aged; Elderly; Prognosis

INTRODUCTION

Pyogenic liver abscess (PLA) is a serious, life-threatening condition, with a mortality rate of 6-14%.[1,2] Along with its increasing incidence worldwide, the mean age of patients with PLA has been increasing.[3-6] In fact, recent reports have emphasized that PLA is primarily a disease of the elderly, who are conventionally defined as those of chronological age ≥65 years.[6,7] Few recent reports specifically focus on elderly patients with PLA.[5,6] Some reports suggest that advanced age might be a prognostic factor for mortality in PLA patients, while others reported elderly PLA patients had better outcome despite requiring longer hospitalization than younger patients.[6,7]

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Considering that the aging population is increasing globally, more studies are needed to examine the clinical features and prognosis of older patients with PLA. Because of the recent increase in life expectancy and because the number of elderly PLA patients is expected to increase further in the future, treatment strategies and clinical outcomes in elderly PLA patients may need to be reconsidered. The effectiveness of percutaneous catheter drainage/percutaneous needle aspiration, the current first-line treatment for PLA, has also not been thoroughly explored in the elderly. Therefore, the aim of the current study is to elucidate the clinical features and outcomes of PLA in elderly patients.

SUBJECTS AND METHODS

1. Patients

This study was approved by the institutional review board of our institution. For data collection, the charts of 602 patients diagnosed with PLA between January 2003 and January 2013 were reviewed retrospectively. For comparison, the patients were divided according to the elderly group (≥65 years) and the non-elderly group (<65 years).

2. Diagnosis of PLA

PLA diagnosis was established according to a combination of clinical features, imaging findings using sonography, CT, or both, and positive bacterial culture results. Radiographic reports were reviewed to determine the location and number of abscesses. The anatomy of the affected liver segment was classified using the Couinaud classification. Presence of more than one abscesses in the same or different lobes was diagnosed as multiple abscesses. Gas-forming liver abscesses were defined as those found to contain air on sonography or CT before aspiration or drainage.

3. Microbiological examination

Blood and abscess cavity cultures were examined. The cultures were isolated for aerobic and anaerobic organisms, employing the standard diagnostic techniques used by the institution's clinical laboratories. Organisms isolated from the abscesses were assumed to be the causative organisms.

4. Liver abscess treatment

The primary therapeutic modality depended on whether percutaneous drainage or open surgery was the first therapeutic procedure performed. If neither of these procedures was performed, the cases were classified as those managed using only antibiotics. The appropriate antibiotic therapy for the abscesses was administered to all patients.

5. Statistical analysis

The patients were divided according to two age groups: ≥65 years (elderly group) and <65 years (non-elderly group), and variables were compared between these groups. Continuous variables were expressed as the mean±standard deviation. The Student t-test and Pearson's chi-squared test or Mann-Whitney test were used to compare the baseline characteristics of the patients. Null hypotheses of no differences were rejected for p-values less than 0.05 or, equivalently, if the 95% confidence interval of the odds ratio estimates excluded 1. Statistical analysis was performed using IBM SPSS Statistics software ver. 20.0 (IBM Co., Armonk, NY, USA).

Table 1. Comparison of Baseline Characteristics between the Patient Groups

Characteristic	Elderly group[a] (n=296)	Non-elderly group[b] (n=306)	p-value
Gender (female)	155 (52.4)	89 (29.1)	<0.001
Age (yr)	73.59±5.98	51.29±9.72	<0.001
Underlying disease			
Diabetes Mellitus	72 (24.3)	74 (24.2)	0.999
Hypertension	147 (49.7)	76 (24.8)	<0.001
Hepatobiliary disease	122 (41.2)	76 (24.8)	<0.001
Malignancy	54 (18.2)	14 (4.6)	<0.001
Hepatobiliary procedure	87 (29.4)	42 (13.7)	<0.001
Alcohol drinker	76 (25.7)	112 (36.6)	0.005
Liver cirrhosis	20 (7.4)	17 (5.6)	0.612
Chronic kidney disease	7 (2.4)	2 (0.7)	0.103
Initial symptom			
Fever	203 (68.6)	241 (78.8)	0.003
Anorexia	68 (23.0)	62 (20.3)	0.488
Abdominal pain	132 (44.6)	125 (40.8)	0.410
Sepsis at admission	24 (8.1)	10 (3.3)	0.013
DIC at admission	2 (0.7)	1 (0.3)	0.339
Initial antibiotics			0.069
3rd generation cephalosporin	251 (84.8)	275 (89.9)	
Quinolone	10 (3.4)	13 (4.2)	
Piperacilline/tazobactam	29 (9.8)	13 (4.2)	
Imipenem	3 (1.0)	0 (0)	
Others	3 (1.0)	5 (1.6)	

Values are presented as n (%) or mean±SD.
DIC, disseminated intravascular coagulation.
[a]≥65 years, [b]<65 years.

RESULTS

1. Patient characteristics

Of the 602 patients enrolled, 296 (49.2%) patients were aged 65 years or older (elderly group) and the remaining 306 (50.8%) patients were aged <65 years (non-elderly group). The mean age was 73.59±5.98 (range, 65-93) years in the elderly group and 51.29±9.72 (range, 11-64) years in the non-elderly group. Associated diseases were more frequently observed in elderly patients. Fever and chills were the most frequent symptoms, followed by abdominal pain and anorexia. Table 1 shows the comparison of baseline clinical characteristics between the patient groups. The percentage of female patients was higher in the elderly group than the non-elderly group (52.4% *vs.* 29.1%, $p < 0.001$). In addition, the percentages of patients with hypertension, hepatobiliary disease, and gastrointestinal malignancy and those who had undergone hepatobiliary procedures were also higher in the elderly group than the non-elderly group (49.7% *vs.* 24.8%, $p < 0.001$; 41.2% *vs.* 24.8%, $p < 0.001$; 18.2% *vs.* 4.6%, $p < 0.001$; 29.4% *vs.* 13.7%, $p < 0.001$; respectively). The percentage of sepsis at admission was also higher in the elderly group (8.1% *vs.* 3.3%, p=0.013). In contrast, the percentages of patients with chronic alcoholism and fever were lower in the elderly group than the non-elderly group (25.7% *vs.* 36.6%, p=0.005; 68.6% *vs.* 78.8%, p=0.003; respectively). The percentages of diabetes mellitus, liver cirrhosis, chronic kidney disease, and other symptoms showed no significant between-group differences. Parenteral empirical antibiotics, cephalosporins, penicillins, quinolone, imipenem, and metronidazole were initially administered to all patients. The antibiotics most commonly used in the elderly patients were third-generation cephalosporin (84.8%) and quinolone (3.4%) with or without metronidazole. Antibiotic therapy was finally administered to all patients on based on the results of their antibiotic susceptibility profiles.

2. Clinical presentations and outcomes

The white blood cell (WBC) count was higher in the elderly group than the non-elderly group (13.44±6.56 *vs.* 12.26±5.89, p=0.021), while CRP level was lower (16.79±9.67 *vs.* 18.80±9.86, p=0.012). The percentage of right lobe abscesses was

Table 2. Comparison of Clinical Presentations and Outcomes between the Patient Groups

Variable	Elderly group[a] (n=296)	Non-elderly group[b] (n=306)	p-value
Laboratory finding			
WBC (/mm^3)	13.44±6.56	12.26±5.89	0.021
PLT (/mm^3)	210.06±136.67	219.62±147.07	0.410
AST (U/L)	121.56±355.26	99.22±263.92	0.381
ALT (U/L)	86.88±217.13	93.06±199.51	0.716
CRP (mg/dL)	16.79±9.67	18.80±9.86	0.012
Radiologic findings			
Abscess size (cm)	5.70±2.57	5.94±2.77	0.271
Multiple abscesses (yes)	73 (24.7)	75 (24.5)	0.999
Abscess site (right lobe)	199 (67.2)	246 (80.4)	<0.001
Gas forming abscess (yes)	18 (6.1)	16 (5.2)	0.725
Microbilology			
Polymicrobial infection (yes)	20 (6.8)	23 (7.5)	0.752
Klebsiella pneumoniae (yes)	93 (31.4)	104 (34.0)	0.487
Culture of resistant organism (yes)	61 (20.6)	44 (14.4)	0.047
Drainage method			
Percutaneous drainage	110 (37.2)	126 (41.2)	0.317
Surgical drainage	2 (0.7)	3 (1.0)	0.999
Duration of admission (day)	16.79±9.67	18.81±9.83	0.698
Total duration of antibiotics (day)	56.94±35.63	59.77±39.02	0.649
Duration of intravenous antibiotics (day)	14.13±0.82	11.73±0.67	0.223
Occurrence of complication (person)	58 (19.6)	39 (12.8)	0.026
Liver abscess related death (person)	9 (3.0)	4 (1.3)	0.170

Values are presented as mean±SD or n (%).
WBC, white blood cell; PLT, platelet.
[a]≥65 years, [b]<65 years.

lower in the elderly patient group than the non-elderly group (67.2% *vs.* 80.4%, $p < 0.001$), while that of inappropriate initial antibiotic treatment was higher (20.6% *vs.* 14.6%, p= 0.047), because more of these patients tested positive for antibiotic-resistant organisms. The treatment methods were antibiotic therapy alone (elderly, 62.1%; non-elderly, 57.8%, $p > 0.05$), percutaneous drainage (37.2% and 41.8%, respectively, $p > 0.05$), and surgical drainage (0.7% and 1%, respectively, $p > 0.05$). The proportion of patients treated using percutaneous or surgical drainage and the length of hospital stay were similar in the two groups. The mortality rate was 3% in the elderly group and 1.3% in the non-elderly group, and this difference was not statistically significant. Other laboratory findings, radiologic findings, drainage procedure and/or surgical intervention used, parenteral antibiotic treatment, and survival outcomes showed no significant between-group differences. However, the incidence of complications was higher in the elderly group than the non-elderly group (19.6% *vs.* 12.8%, p=0.026). Table 2 summarizes the comparison of clinical presentations and outcomes between the patient groups.

3. Complications

Adverse events occurred during admission in 58 cases (19.6%) in the elderly group and 39 cases (12.7%) in the non-elderly group. The incidence of each complication were similar between the elderly and the non-elderly patients, except for septic shock (8.1% *vs.* 2.3%, p=0.001) and cardiovascular conditions such as acute coronary syndrome and cerebral infarction (2% *vs.* 0%, p=0.014). The comparison of complications between the patient groups is summarized in Table 3.

4. Microbial examination

The species of bacteria isolated from the patients' samples and antibiotic-resistance are summarized in Table 4. In the elderly group, *Klebsiella pneumoniae* was the most commonly isolated species from blood (21.6%), followed by *Escherichia coli* (4.1%). In the case of pus, however, this trend was reversed: *E. coli* was the most commonly isolated species (14.5%), followed by *K. pneumoniae* (12.2%). Antibiotic-resistant organisms were isolated in 61 (20.6%) elderly patients and 44 (14.4%) non-elderly patients. Extended-spec-

Table 3. Comparison of Complications between the Patient Groups

Variables	Elderly group[a]	Non-elderly group[b]	p-value
Septic shock	24 (8.1)	7 (2.3)	0.001
Septic pneumonia	4 (1.4)	3 (1.0)	0.482
Metastatic CNS infection	1 (0.3)	1 (0.3)	0.999
Metastatic psoas abscess	2 (0.7)	0 (0)	0.241
Endopthalmitis	5 (1.7)	7 (2.3)	0.773
Rupture of liver abscess	8 (2.7)	4 (1.3)	0.255
Cardiovascular disease	6 (2.0)	0 (0)	0.014
Others	12 (6.1)	17 (5.6)	0.845

Values are presented as n (%).
CNS, central nervous system.
[a]≥65 years, [b]<65 years.

Table 4. Bacterial Spectrum and Antibiotics-resistance of Culture Results

Organism	Elderly group[a] (n=296)			Non-elderly group[b] (n=306)		
	Blood	Pus	Antibiotics resistance	Blood	Pus	Antibiotics resistance
No growth	178 (60.1)	205 (69.3)		203 (66.8)	166 (54.6)	
Klebsiella pneumoniae	64 (21.6)	36 (12.2)	38 (12.8)	52 (17.1)	43 (14.1)	31 (10.1)
Escherichia coli	12 (4.1)	43 (14.5)	8 (2.7)	6 (2.0)	75 (24.7)	5 (1.6)
Citrobacter	1 (0.3)	2 (0.7)	1 (0.3)	0 (0)	6 (2.0)	0 (0)
Pseudomonas	4 (1.4)	2 (0.7)	2 (0.7)	3 (1.0)	0 (0)	0 (0)
Staphyllococcus	6 (2.0)	3 (1.0)	4 (1.4)	7 (2.3)	6 (2.0)	3 (1.0)
Streptococcus	0 (0)	2 (0.7)	0 (0)	2 (0.7)	1 (0.3)	2 (0.6)
Bacteroides	1 (0.3)	2 (0.7)	0 (0)	0 (0)	2 (0.7)	0 (0)
Bacillus	1 (0.3)	0 (0)	2 (0.7)	0 (0)	0 (0)	0 (0)
Brevibacterium	3 (1.0)	0 (0)	0 (0)	1 (0.3)	0 (0)	1 (0.3)
Enterobacter	0 (0.3)	1 (0.3)	3 (1.0)	1 (0.3)	1 (0.3)	1 (0.3)
Enterococcus	2 (0.7)	0 (0)	3 (1.0)	1 (0.3)	2 (0.7)	1 (0.3)
Proteus vulgaris	1 (0.3)	0 (0)	0 (0)	0 (0)	1 (0.3)	0 (0)

Values are presented as n (%).
[a]≥65 years, [b]<65 years.

trum β-lactamase (ESBL) positive *K. pneumoniae* was the most commonly isolated resistant organism (11.5%), followed by ESBL positive *E. coli* (2.2%).

DISCUSSION

In the current study, detailed clinical information on manifestations, imaging and laboratory findings, microbiological studies, treatment, and outcome were assessed to examine the differences between older and younger PLA patients. We found that elderly PLA patients had more atypical presentations; underlying diseases (such as hypertension, gastrointestinal cancer, and biliary disease) but a similar clinical outcome compared to younger patients, despite having more complications, such as cardiovascular disease and septic shock during hospital stay. Regarding high incidence of antibiotic-resistant pathogens of PLA in elderly patients, use of antibiotics covering drug resistant organisms should be considered earlier, especially in elderly patients with previous history of antibiotic use and severe septic condition, and percutaneous drainage should be actively performed to isolate pathogen and improve clinical outcomes despite poor clinical condition at admission.

Consistent with a previous report, the elderly group included more female patients than the non-elderly group.[8] This age-related trend in gender distribution reflects the longer life expectancy of women than men. Further, it is not surprising that comorbidities such as hypertension, biliary disease, gastrointestinal malignancy, and cardiovascular disease were found more commonly in elderly patients, as these are conditions are associated with old age. Although the incidence of clinical manifestations of PLA, including fever, abdominal pain, and anorexia, was similar between the groups, patients in the elderly group were less likely to develop fever than those in the non-elderly group. Two previous reports on PLA in the elderly suggested that PLA in the elderly is characterized by atypical clinical presentations and misleading results from diagnostic tests.[9,10] We found that the WBC count was higher in the elderly group than the non-elderly group (13.44±6.56 *vs.* 12.26±5.89), while the CRP level was lower (16.79±9.67 *vs.* 18.80±9.86). The differences in the WBC counts can be explained by the fact that atypical symptoms in elderly patients could delay the definite diagnosis of PLA and they may present with more severe infection at admission. In addition, low levels of CRP may be produced in response to the liver interleukin-6 levels in elderly patients. Consistent with the results of a previous study, we found that in both groups, most abscesses were single and were located in the right hepatic lobe, although right lobe involvement was less dominant in the elderly group.[11] This finding may be related to the higher incidence of biliary tract diseases such as bile duct stones in the elderly group.[12]

In the current study, *K. pneumoniae* was the most commonly isolated species from both pus and blood. This finding is mostly consistent with those of previous studies.[13,14] A high percentage of patients in this study tested positive for antibiotic resistance, which is consistent with previous reports, and the percentage of antibiotic-resistance was significantly higher in the elderly group than in the non-elderly group.[5,6] This difference can be explained by the fact that more elderly patients had a history of antibiotic exposure. The indiscriminate use of antibiotics in clinical practice nowadays may have led to a higher proportion of culture positivity of antibiotic-resistant organisms, which may in turn have led to inappropriate initial administration of antibiotics in the elderly patients. In addition, older age and underlying malignancy are known risk factors for antibiotic resistance in pathogens.[15]

As reported previously as well, in our study no significant differences in the therapeutic procedures performed or antibiotics administered, duration of hospital stay, or duration of intravenous antibiotic use were observed between the groups.[12] The average inhospital PLA mortality rate in the current study was 2.2%, one of the lowest reported mortality rates for PLA, and no significant difference in mortality rate was observed between the groups. Other studies have also shown a progressive decrease in mortality rates.[16] This may be due in part to improved imaging and diagnostic techniques as well as the increased use of percutaneous drainage. In the current study, percutaneous drainage was actively performed in non-elderly patients as well as in elderly patients without complication (37.2% *vs.* 41.8%, p=0.371), resulting in improved survival outcome.

In previous studies reported in South Korea, mean age of PLA patients was about thirties to forties, mortality rate of PLA was approximately 20%, and major complications of PLA were intra-abdominal complications such as peritonitis, subphrenic abscess, and rupture of abscess in the 1970s.[17-19] However, mean age of PLA has been increasing and mortality

rate has shown a significant decrease to less than 2% by improvement of antibiotic treatment and drainage procedure.[17-22] In the current study, elderly patients had more complications than younger patients. While not inclined to pulmonary complications, more various complications (metastatic infection, cardiovascular events) occurred. Septic shock rate was high (8.1%) in elderly patients. Regarding pathogens of PLA, Ameba and *E. coli* were most common in the past. However, *Klebsiella* has become the most common pathogen and drug-resistant pathogens have shown a recent increase.[20-23] In the current study, *Klebsiella* was the most common pathogen and prevalence of antibiotic resistance was higher (20.6%) in elderly patients than younger patients (14.3%). Among resistant organisms, ESBL positive *K. pneumoniae* was the most common (11.5%), followed by ESBL positive *E. coli* (2.2%).

This study has several limitations. First, because this was a retrospective, single-center analysis, our results may not be suitable for generalization across other patient populations. Further, clinical presentation data obtained from medical records may be inadequate, which could affect the validity of the findings.

In conclusion, elderly patients with PLA tended to show more atypical PLA presentation and complications than younger patients. Despite being in poorer clinical condition at admission, clinical outcomes of the elderly were not inferior to those of the younger patients Therefore use of antibiotics covering drug resistant organisms should be considered earlier, and percutaneous drainage should be actively performed to isolate pathogen and improve clinical outcomes. Although large-scale prospective studies are needed to confirm our findings, clinicians should be aware of these age-related differences in PLA and modify treatment and management strategies accordingly.

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