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Pyogenic liver abscess in the elderly: clinical features, outcomes and prognostic factors

SHIUAN-CHIH CHEN[1,2,3], YUAN-TI LEE[3,4,5], CHI-HUA YEN[1,2,3,5], KUANG-CHI LAI[5,6], LONG-BIN JENG[6], DING-BANG LIN[7], PO-HUI WANG[3,5], CHUN-CHIEH CHEN[1,3], MENG-CHIH LEE[1,2,5,8], WILLIAM R. BELL[9]

[1]Department of Family and Community Medicine, Chung Shan Medical University Hospital, Taichung, Taiwan
[2]Department of Geriatric Medicine, Chung Shan Medical University Hospital, Taichung, Taiwan
[3]School of Medicine, Chung Shan Medical University, Taichung, Taiwan
[4]Department of Internal Medicine, Chung Shan Medical University Hospital, Taichung, Taiwan
[5]Institute of Medicine, Chung Shan Medical University, Taichung, Taiwan
[6]Department of Surgery, China Medical University Hospital, Taichung, Taiwan
[7]School of Medical Laboratory and Biotechnology, Chung Shan Medical University, Taichung, Taiwan
[8]National Project for Excellence in Geriatric Care Education (NPEGCE), Chung Shan Medical University, Taichung, Taiwan
[9]Division of Hematology, Department of Medicine, The Johns Hopkins University School of Medicine, Baltimore, MD, USA

Address correspondence to: C.-C. Chen, Faculty of Medicine, Chung Shan Medical University School of Medicine, No. 110, Sec. 1, Jianguo N. Rd., South District, Taichung City 40201, Taiwan. Tel: (+886) 4-24739595, ext. 34971; Fax: (+886) 4-23248137; Email: cccy218@yahoo.com.tw

Abstract

Background: pyogenic liver abscess (PLA) is a potentially life-threatening disease in middle-to-old aged persons.
Objective: to compare the differences in clinical features and outcomes between older and younger PLA patients, and to identify predictors of outcomes in older patients.
Design: retrospective chart review of all PLA patients between July 1999 and June 2007.
Setting: a 1,600-bed primary and tertiary care centre.
Subjects: in total, 339 patients were enrolled and included 118 ≥65 years of age (the elderly group) and 221 patients <65 years of age (the non-elderly group).
Methods: clinical features, laboratory, imaging and microbiologic findings, treatment and outcomes for each of the included patients were collected. The predictor of outcome was determined using logistic regression and purposeful selection of covariates.
Results: the elderly group had a higher APACHE II score on admission, a biliary abnormality, a malignancy, a pleural effusion, polymicrobial, anaerobic or multi-drug-resistant isolates, inappropriate initial antibiotics, a longer hospitalisation and a longer parenteral antibiotic treatment period than the non-elderly group, whereas the non-elderly group was more likely to be alcoholic men with cryptogenic origin of abscess and *Klebsiella pneumoniae* infection. There was no difference in case fatality between the elderly (13.6%) and non-elderly (8.6%) groups despite the elderly group having a poorer host status on admission. In multivariate analysis, age ($P = 0.028$) and APACHE II score at admission ≥15 ($P = 0.001$) were risk factors, but *K. pneumoniae* infection ($P = 0.012$) was a protective factor for fatality in older PLA patients.
Conclusions: these data suggest that older PLA patients wound have a fair outcome compared to younger patients, but require longer hospitalisations.

Keywords: *pyogenic liver abscess, elderly, risk factor, prognosis*

Introduction

Ochsner *et al.* [1] reported the first comprehensive study of pyogenic liver abscesses (PLAs) in 1938, which were predominantly diagnosed in young men, were associated with pyelophlebitis and accompanied by a high fatality rate (77%). With the advances in diagnostic techniques and therapeutic modalities, the incidence of PLA has increased and the case-fatality rate has gradually declined, but remains within the range of 6–35% [2–11]. Further, the mean age of PLA patients has increased since 1938 and PLA has become a disease of the middle-aged and elderly with a reported mean age

of 47–65 years [2–11]. This change in patient demographics likely reflects a change in the predominant aetiology. Some investigators have hypothesised that advanced age might be one of the prognostic factors for mortality in PLA patients [4]. While several groups have attempted to explore the discrepancies in clinical features and prognosis between younger and older patients [8, 12, 13], there was either lack of an appropriate comparison group or a small sample size in these reports. In addition, the effectiveness of percutaneous catheter drainage (PCD)/percutaneous needle aspiration (PNA), the current first-line treatment for PLA, remains unclear in older patients.

In this study, detailed clinical information including clinical manifestations, imaging and laboratory findings, microbiologic studies, treatment and outcome was assessed to explore the differences between older and younger patients and to identify prognostic factors in older PLA patients. We also reported our clinical experience of PCD/PNA in these patients.

Methods

Study subjects and setting

Between 31 July 1999 and 30 June 2007, the medical records of consecutive patients ≥18 years who were discharged with a diagnosis of PLA from the China Medical University Hospital in Taichung, Taiwan, were examined. Patients were identified using a systematic search of the medical records for the diagnostic code, liver abscess (LA). All PLA patients who underwent abdominal ultrasonography (US) and/or computerised axial tomography (CT) scans with contrast enhancement were included in the study. Patients were included in the study if they met both of the following criteria: (i) one or more space-occupying lesions in the liver diagnosed by imaging studies (i.e. abdominal US and/or CT scans), and (ii) bacterial pathogens identified in the blood and/or LA cultures. Of the 381 patients with the diagnostic code of LA, 42 were excluded due to amoebic LAs ($n = 6$), parasitic LAs ($n = 3$), mycotic LAs ($n = 4$), tuberculous LA ($n = 1$), necrotic tumours ($n = 2$), infected bilomas ($n = 3$) and negative results from cultures of blood and LAs ($n = 23$). The remaining 339 patients fulfilled the inclusion criteria and were divided into two groups: patients ≥65 years of age were included in the elderly group and patients <65 years of age were included in the non-elderly group. This study was approved by the institutional review board of the hospital.

Data collection and definition of variable

Please see this section in Appendix 1 of the supplementary data available on *Age and Ageing* online.

Statistical analysis

Descriptive statistics were used to characterise the study subjects and were summarised as the mean ± standard deviation or the median (25th–75th percentiles) for continuous data and as the percentage for categorical data. The Student's *t*-test or the Mann–Whitney *U*-test was employed to compare continuous variables between the groups, where appropriate. The chi-square test or the Fisher exact test was performed to compare categorical variables between groups. Outcomes were analysed between the two groups using logistic regression with adjustment for all baseline and clinical covariates, which included all demographic, clinical presentation, imaging, laboratory, microbiologic and therapeutic variables. We used purposeful selection of covariates to assess prognostic factors for PLA in older patients and to construct the logistic regression model using variables that were significant in bivariate analyses and retained these variables in the model with *P*-values of 0.20 or less. A value of ≥20% was used as an indicator of an important change in a coefficient. All of the initial models included all baseline and clinical covariates. The purposeful selection method for the covariates and the modelling process were described by Hosmer *et al.* [17]. Odds ratios and 95% confidence intervals were also estimated. All statistical analyses were performed using the SAS software, version 8.2 (SAS Institute Inc., Cary, NC, USA); a two-sided *P*-value of <0.05 was considered statistically significant.

Results

Demographic data, underlying diseases, clinical features, microbiological, imaging and laboratory findings

Of the 339 patients, 118 were included in the elderly group while the remaining 221 patients were included in the non-elderly group. The median ages of the elderly and non-elderly groups were 73.0 years (25th–75th percentiles, 69.0–78.0 years) and 51.0 years (25th–75th percentiles, 41.5–58.0 years), respectively. Older PLA patients were more likely to have a higher APACHE II score on admission, a biliary abnormality and a malignancy than younger patients. In contrast, younger patients were more likely to be males and have alcoholism and a cryptogenic aetiology compared to older patients. Symptoms and signs on admission were similar between the groups, except that older patients had significantly less right upper quadrant (RUQ) tenderness than the young patients ($P < 0.05$) (Table 1).

The species of bacteria isolated from PLA patients are summarised in Table 2. In the elderly group, 88 isolates were obtained, and the recovery frequency from bacterial blood cultures was 66.7% (76/114 patients). In the younger patients, there were 151 isolates and the recovery frequency was 66.1% (144/218 patients). The proportion of recovery from abscess cultures was 96.4% (108/112 patients) with 175 isolates in the older patients and 95.5% (193/202 patients) with 234 isolates in the younger patients. The percentage of recovery from abscess cultures was significantly higher than blood cultures in the two groups ($P < 0.0001$). Polymicrobial infections, anaerobes, multi-drug-resistant (MDR) isolates, *Escherichia coli* infection and pleural effusion were more commonly identified in the older patients than the younger patients, whereas

Table 1. Significant baseline characteristics, underlying diseases and clinical features of the elderly and non-elderly groups at the time of admission

Variable	Elderly group ($n = 118$)	Non-elderly group ($n = 221$)	*P*-value
Gender, male, no. (%)	60 (50.8)	151 (68.6)	0.001
APACHE II score at admission	12.6 ± 5.3	8.0 ± 5.4	<0.0001
Underlying condition[a], No. (%)			
Biliary stone disorder[b]	52 (44.1)	49 (22.2)	<0.0001
Malignancy	24 (20.3)	17 (7.7)	0.001
Alcoholism	5 (4.2)	39 (17.6)	<0.0001
Origin of abscess			
Biliary origin[c]	44 (37.3)	58 (26.3)	0.035
Cryptogenic origin	69 (58.5)	153 (69.2)	0.047
Clinical Signs[a], no. (%)			
RUQ tenderness	53 (44.9)	126 (57.0)	0.034
Microbiologic characteristics			
Polymicrobial infection[d]	37 (31.4)	27 (12.2)	<0.0001
Anaerobic infection[e]	22 (18.6)	16 (7.2)	0.002
MDR isolates	25 (21.2)	17 (7.7)	<0.0001
E. coli infection[f]	36 (30.5)	24 (10.9)	<0.0001
K. pneumoniae infection[g]	78 (66.1)	187 (84.6)	<0.0001
Pleural effusion	65 (55.1)	97 (43.9)	0.049

Data are presented as mean ± standard deviation, unless otherwise indicated. APACHE = Acute Physiology and Chronic Health Evaluation; RUQ = right upper quadrant.

[a]When patients fit into more than one category, they were counted in each category.

[b]Biliary stone disorder: cholelithiasis, choledocholithiasis and/or hepatolithiasis.

[c]Biliary origin: cholecystitis or purulent cholangitis with/without malignancy.

[d]Polymicrobial infection: mixed bacterial flora was cultured in blood and/or abscess cultures.

[e]Anaerobic infection: anaerobic isolates were cultured in blood and/or abscess cultures.

[f]*E. coli* infection: *E. coli* was cultured in blood and/or abscess cultures.

[g]*K. pneumoniae* infection: *K. pneumoniae* growing in blood or abscess cultures.

Klebsiella pneumoniae infection was more frequently observed in the older patients compared to the younger patients (Table 1). No differences in abscess characteristics and laboratory findings between the groups existed and the detailed demographic data and clinical findings of the two groups are shown in Appendices 2 and 3, available on *Age and Ageing* online.

Treatment, morbidity and clinical outcome

Each patient was initially treated with one of four therapeutic methods: (i) antibiotic therapy only, (ii) antibiotics plus image-guided PNA, (iii) antibiotics plus image-guided PCD or (iv) antibiotics plus surgical intervention. The initial treatment for PLA was based on the attending clinician's preference. Additional intervention was required in seven older patients (three with initial antibiotics alone, one with initial PNA and three with initial PCD) and in nine younger patients (five with initial antibiotics alone, one with initial PNA and three with initial PCD).

Table 2. Bacterial spectrum of PLA patients in both the elderly and non-elderly groups

	Elderly group ($n = 118$)		Non-elderly group ($n = 221$)	
Organisms	Blood ($n = 76$)	Abscess ($n = 108$)	Blood ($n = 144$)	Abscess ($n = 193$)
Gram-negative aerobes				
Klebsiella pneumoniae	52	72	114	164
Escherichia coli	13	32	11	20
Klebsiella oxytoca	3	2		1
Pseudomonas spp.	1	7	1	4
Proteus spp.	1	5	1	4
Aeromonas spp.	1	1		2
Acinetobacter spp.	1	1		
Citrobacter spp.		3		2
Enterobacter spp.		2	2	1
Morganella spp.		2		2
Edwardsiella tarda		1		
Burkholderia cepacia			1	
Pantoea agglomerans				1
Unidentified bacilli			1	1
Gram-positive aerobes				
Streptococcus spp.		13	3	10
Enterococcus spp.	4	6	1	4
Staphylococcus spp.	3	4	4	1
Gemella morbillorum	1	1		
Anaerobes				
Bacteroides spp.	6	12	10	5
Prevotella spp.	2			5
Peptostreptococcus spp.		5		2
Bifidobacterium spp.		2	1	2
Fusobacterium spp.		2		2
Clostridium spp.		1	1	1
Propionibacterium spp.		1		
Total isolates	88	175	151	234

All patients initially received parenteral empirical antibiotics, including cephalosporins, penicillins, aminoglycosides and metronidazole. A total of 72 patients (61.0%) in the elderly group and 145 patients (65.6%) in the non-elderly group initially received either first- or second-generation cephalosporins with or without gentamicin. As depicted in Table 3, the frequency of inappropriate initial antibiotic treatment was higher in the older patients than in the younger patients. All patients were subsequently administered antibiotic therapy based on the results of the antibiotic susceptibility profiles. The length of hospitalisation and parenteral antibiotic treatment was longer in the older patients than in the younger patients, but there were no significant differences in the length of hospitalisation ($P = 0.086$) and parenteral antibiotic treatment ($P = 0.298$) between the two groups after multivariate adjustment. The case-fatality rates in the older and the younger patients were 13.6% and 8.6%, respectively, but the difference between the groups did not reach statistical significance before adjustment ($P = 0.153$) and after multivariate adjustment ($P = 0.070$).

Among the 301 patients who underwent PCD/PNA as initial therapy, the older patients had a higher proportion of inappropriate initial antibiotic treatment ($P = 0.002$),

Table 3. Morbidity, treatment and clinical outcome in the elderly and the non-elderly groups

Variable	Elderly group ($N = 118$)	Non-elderly group ($N = 221$)	P–value
Metastatic/contiguous infection, no. (%)	16[a] (13.6)	29[b] (13.1)	0.910
Abscess rupture, no. (%)	4 (3.4)	9 (4.1)	1.000
Duration of diagnosis made after admission, days	1.4 ± 2.2	1.5 ± 4.2	0.822
Initial treatment method, no. (%)			0.567
Antibiotics alone	10 (8.5)	23 (10.4)	
Invasive procedure[c] plus antibiotics	108[d] (91.5)	198[e] (89.6)	
Inappropriate initial antibiotics, no. (%)	21 (17.8)	14 (6.3)	0.001
Subsequent treatment needed, no. (%)	7 (5.9)	9 (4.1)	0.442
Time to defervesce after admission	8.6 ± 13.6	7.6 ± 8.0	0.469
Hospital stay	25.5 ± 22.7	19.5 ± 10.7	0.008
Length of intravenous antibiotics	21.7 ± 20.0	18.1 ± 10.8	0.033
Length of total (intravenous + oral) antibiotics	38.2 ± 26.1	39.9 ± 20.9	0.540
Recurrence, no. (%)	7 (5.9)	9 (4.1)	0.442
Death, no. (%)	16 (13.6)	19 (8.6)	0.153

Data are expressed as mean ± standard deviation unless otherwise indicated.
[a]Elderly group: septic endophthalmitis ($n = 1$), subphrenic abscess ($n = 1$), septic pulmonary embolism ($n = 1$), pneumonia ($n = 2$), splenic abscess ($n = 3$), subcutaneous/muscular abscess ($n = 2$), peritonitis ($n = 1$), osteomyelitis ($n = 1$) and pleural empyema ($n = 4$).
[b]Non-elderly group: septic endophthalmitis ($n = 2$), subphrenic abscess ($n = 2$), meningitis ($n = 2$), septic pulmonary embolism ($n = 5$), splenic abscess ($n = 3$), subcutaneous/muscular abscess ($n = 5$), osteomyelitis ($n = 1$) and pleural empyema ($n = 9$).
[c]Invasive procedure: percutaneous needle aspiration (PNA), percutaneous catheter drainage (PCD) or surgical intervention.
[d]Of the 108 patients, 8 underwent PNA and 100 underwent PCD.
[e]Of the 198 patients, 17 underwent PNA, 176 underwent PCD and 5 were managed surgically.

and a longer duration of hospitalisation ($P = 0.001$) and intravenous antibiotics administration ($P = 0.024$) than the younger patients (Appendix 4, available on *Age and Ageing* online). The results of this subgroup analysis were similar to the total cases analysis.

Analysis of prognostic factors related to outcome in older patients with pyogenic liver abscess

The prognostic factors for outcomes in older PLA patients were identified using logistic regression models and purposeful selection of covariates. In the final model, an APACHE II score ≥15 on admission ($P = 0.007$), time to defervescence >7 days post-admission ($P = 0.006$) and pro-thrombin time >13.1 s ($P = 0.008$) were associated with hospitalisation ≥3 weeks. An APACHE II score ≥15 on admission ($P = 0.001$) and age ($P = 0.028$) were risk factors, but *K. pneumoniae* infection ($P = 0.012$) was a protective factor for case fatality via multivariate analysis (Appendix 5, available on *Age and Ageing* online).

Discussion

Several key findings were identified in this study. First, some discrepancies in clinical features existed between the older and younger PLA patients. As described in the literature [8, 12, 13], older PLA patients are more likely to have a biliary abnormality/aetiology or underlying malignancy, whereas younger PLA patients are more likely to be males, to have RUQ tenderness, alcoholism and a cryptogenic aetiology. Polymicrobial or anaerobic infections with MDR organisms, a pleural effusion, inappropriate initial antibiotic selection and a greater severity of illness on admission occur more frequently in older PLA patients than younger patients. Indeed, these are novel findings that have not been reported previously in the literature. Second, the case fatality in older PLA patients was related to host conditions, rather than to characteristics related to the LA itself. Interestingly, older PLA patients with a positive culture for *K. pneumoniae* had a better prognosis than older patients without *K. pneumoniae*.

The published studies [8, 12, 13] regarding older PLA patients have several limitations, primarily related to small sample sizes. Each of the three studies included <20 patients, and these studies lack an analysis of bacterial characteristics, detailed information regarding outcome or a comparison group of younger patients. Our study included 118 older PLA patients, which makes it the largest study of its kind and provides us with adequate power to make a comparison between older and younger patients. However, a potential limitation to our study is the fact that this was a retrospective study based on the review of medical records. Clinical presentation according to medical records may inevitably have insufficient information that could impact the validity and attenuate the findings.

The diagnosis of PLA is challenging due to its vague presenting symptoms/signs and non-specific laboratory findings. Moreover, this study revealed that presenting RUQ tenderness in older patients occurred less frequently than in the young despite the higher frequency of biliary aetiology/disorders in older patients. However, our data did not support the postulation by Smoker *et al.* [8], as this subtle feature in older patients may contribute to a delay in PLA diagnosis. The mean duration of symptoms prior to admission was 5.3 days and the mean time until diagnosis of PLA was made after admission was 1.4 days in older patients, which is shorter than the corresponding times reported in previous studies [8, 12, 13]. Additionally, there were no differences in the duration of symptoms prior to admission and diagnosis made after admission between the older and younger groups. It is possible that the improvement and availability of diagnostic imaging studies, such as US and CT scans, and a high index of suspicion of PLA contributed to this decrease in the time to diagnosis.

Our data revealed that age did not affect the recovery frequency of abscess and blood cultures which is in contrast to the observations of Smoger *et al.* [8] that older patients were less likely to have positive results of blood cultures than the young. This is likely a reflection on the improvement in

current techniques and procedures for culturing pathogenic organisms. The yield of MDR isolates in younger patients was rare, whereas MDR was relatively commonly identified in older patients. This may lead to a higher proportion of inappropriate initial empirical administration of antibiotics in elderly patients. Older age and underlying malignancy have been shown to be the risk factors for developing antibiotic-resistant pathogens [18, 19], which may partly explain the higher incidence of MDR isolates in older patients. Information regarding antibiotic usage prior to admission was not obtained in this retrospective study, which may weaken this finding. Underlying malignancy, which was more prevalent in older PLA patients, has been regarded as a risk factor for developing anaerobic infections [20, 21]. This may explain why anaerobic pathogens were more frequently recovered in older patients than in the young. This finding implies that initial antibiotics with anaerobic coverage may be indicated in older PLA patients, particularly in patients with malignancy.

With the advent and widespread availability of imaging modalities, image-guided PCD/PNA has become the treatment of choice for PLA in most institutions, as they are less invasive compared with surgical intervention; the reported case-fatality rate of PCD/PNA as a primary treatment ranged from 0 to 15% [5, 9, 10, 22–26]. The case-fatality rate in older patients who underwent image-guided PCD/PNA herein was 13.7%, which is located within the reported range. The difference in case-fatality rates between the older and younger groups did not reach significance in our study, but a larger sample size and prospective design is needed to verify this. We also found that older patients required a longer hospitalisation compared with younger patients, although it was not significant after adjustment. This finding implies that the longer hospitalisation needed in older patients may be related to correct host conditions, rather than to treat the LA *per se*. This supposition is supported by the following: (i) no difference existed in the duration of drainage between the two groups and (ii) there was a higher APACHE II score on admission (one of risk factors for prolonged hospitalisation) in older patients. Several groups have advocated that PLA should be treated with PCD/PNA plus a combination of 2 to 3 weeks of parenteral and a subsequent 4 to 6 weeks of oral antibiotics [5, 7, 27, 28]. The duration of antimicrobial therapy was based on the clinician's individual decision in this study, which likely explains why there was no difference in the duration of total antibiotic treatment between the two groups.

Several studies to identify prognostic factors for case fatality in PLA patients have been performed, yet discrepancies exist regarding this issue [3, 4, 7, 9–11, 29]. No other studies identifying prognostic factors for old PLA patients have been reported. Age and an APACHE II score $\geq$15 on admission were the risk factors for case fatality in older PLA patients. On the other hand, *K. pneumoniae* infection was found to be a protective factor. This finding is similar to the results of some other reports in which *K. pneumoniae* PLA was relatively benign with a low case-fatality rate and a good clinical response [29, 30].

In conclusion, older PLA patients were significantly different from the young in terms of the sex ratio, the severity of illness on admission, underlying diseases, the origin of the abscess, the presence of RUQ tenderness or pleural effusion and the frequency of polymicrobial, anaerobic or MDR isolates. Older PLA patients may tolerate management with PCD/PNA well, despite having a poorer clinical condition on admission. Clinicians should apply an aggressive approach as soon as possible for older patients exhibiting a poor response to primary treatment, particularly in those with a greater severity of illness on admission.

Key points

- There were differences in sex ratio, the severity of illness on admission, underlying diseases, the origin of the abscess, the presence of RUQ tenderness or pleural effusion, and the frequency of polymicrobial, anaerobic, or MDR isolates between the older and younger PLA patients.
- Older PLA patients would have a fair outcome compared to younger patients but require longer hospitalizations.
- Older PLA patients would tolerate management with PCD/PNA well, despite having a poorer clinical condition on admission.

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Conflicts of interest

All authors declare no conflict of interest.

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Supplementary data

Supplementary data are available at *Age and Ageing* online.

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