Comparison of pyogenic liver abscesses of biliary and cryptogenic origin

An eight-year analysis in a University Hospital

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Summary

Objectives: The aim of this study is to delineate the clinical features of pyogenic liver abscesses of biliary and cryptogenic origin, and to compare the differences in outcome of patients between the two groups.

Methods: We studied 86 patients, aged 19 years or older, with pyogenic liver abscess admitted to Chung Shan Medical University Hospital, Taichung, Taiwan, between January 1996 and December 2003. The demographic data and medical information of the patients were reviewed and recorded. Of the 86 patients, 34 were classified into the biliary group and 52 were classified into the cryptogenic group.

Results: Patients with pyogenic liver abscesses of biliary origin had a higher frequency of underlying malignancy and Murphy's sign compared to those with pyogenic liver abscesses of cryptogenic origin. With respect to specific pathogens, *Escherichia coli* were more prevalent in the biliary group while *Klebsiella pneumoniae* were more prevalent in the cryptogenic group. Anaerobic isolates were less frequently cultured in the cryptogenic group than in the biliary group. After adjustment for age, sex, and the duration of symptoms before admission, there was no difference in mortality between both groups (biliary *vs* cryptogenic: 15% *vs* 8%; adjusted OR, 1.43; 95% CI, 0.24–8.25; $p = 0.899$). After adjustment for confounders, patients in the biliary group had higher frequencies of time to defervesce >1 week after admission (68% *vs* 40%; adjusted OR, 3.05; 95% CI, 1.09–9.04, $p = 0.030$) and hospital stay >3 weeks (47% *vs* 15%; adjusted OR, 4.34; 95% CI, 1.45–13.91; $p = 0.007$) than those in the cryptogenic group.

Conclusions: This report highlights that pyogenic liver abscesses of cryptogenic origin had a benign clinical response, which was associated with shorter duration of hospitalisation and time to defervesce after admission, compared to those of biliary origin.

Key words: pyogenic liver abscess; aetiology; biliary tract diseases; cryptogenic origin

Introduction

The physiopathologic characteristics of pyogenic liver abscess have changed during the past 70 years. In 1938, Ochsner et al. reported that 45% of patients with pyogenic liver abscesses had primary abdominal disease with pylephlebitis, associated with high morbidity and mortality rates [1]. Since the introduction of antibiotics, the aetiology of pyogenic liver abscess has shifted and has been most frequently associated with biliary tract disease [2–6]. With the availability of antibiotic agents, microbiology methods, imaging techniques and therapeutic modalities, the outcome of pyogenic liver abscess has been improved during the last 20 years [3–12]. Recent reports have noted an increase in the frequency of patients with cryptogenic liver abscesses [13, 14]. Moreover, some investigators reported that the majority of patients with pyogenic liver abscesses, who underwent abdominal computerised tomography (CT) scans and/or ultrasound (US) examinations, were of cryptogenic origin [13, 15, 16]. However, the predisposing condition, clinical features and outcome of pyogenic liver abscesses of cryptogenic origin are far less reported compared to those of other origins.

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The objective of this study was to delineate the clinical manifestations, characteristics of abscesses, microbiological studies, and outcome of pyogenic liver abscesses of biliary and cryptogenic origin, and to assess the differences in the outcome between the two groups.

Methods

Study patients

Consecutive patients aged 19 years or older with a final diagnosis of pyogenic liver abscess admitted to the Chung Shan Medical University Hospital, Taichung, Taiwan, between January 1996 and December 2003 were included in this study. The Chung Shan Medical University Hospital is a 1300-bed tertiary care teaching hospital receiving patients from central Taiwan. The diagnosis of pyogenic liver abscess was established after imaging one or more discrete abscess cavities of the liver, and identification of bacterial organisms isolated from blood and/or abscess cultures. Suspected amoebic liver abscesses were excluded from this study if no yield from any cultures and positive visualisation of wet-mount examinations or indirect haema-aglutination antibody (IHA) titers greater than 1:64 [17] were present. We also excluded patients with fungal and parasitic liver abscesses from this analysis. Imaging evaluation included chest and abdominal x-ray, endoscopic retrograde cholangiopancreatography (ERCP), US and/or CT scans with contrast enhancement. One hundred and six patients were enrolled by a systematic search of the patients' records for diagnostic codes and the patients' age at admission. From these, 13 patients were excluded because of the following conditions: incomplete medical record (1 patient), fungal abscess (1 patient), parasitic abscess (1 patient), amoebic abscesses (3 patients), and negative for both blood and abscess cultures (7 patients). The remaining 93 patients with pyogenic liver abscess were identified and treated at the Chung Shan University Hospital during the study period.

Data collection

Demographic data and medical information were retrospectively collected. The medical information included underlying diseases, clinical features, laboratory data, radiographic and microbiological findings, methods and agents of initial treatment, and outcome. Abscess material was obtained by image (CT or US)-guided percutaneous needle aspiration (PNA) (diagnostic or therapeutic), image-guided percutaneous catheter drainage (PCD), or direct surgical intervention, and at least 2 sets of blood cultures were obtained. The specimens obtained were processed with gram stain, bacterial cultures (standard aerobic and anaerobic diagnostic methods) and tests for antibiotic susceptibility. Antibiotic susceptibility testing was performed by agar disk diffusion using antibiotic disks (BD BBL™ Sensi-Disc™ Antimicrobial Susceptibility Test Discs, Sparks, MD, USA), selected according to the microorganism isolated. Results were evaluated according to the criteria of the National Committee for Clinical Laboratory Standards and the procedure was periodically updated [18, 19].

After the cultures of blood and/or liver abscess aspirate were obtained, empirical broad-spectrum antibiotics were administered parenterally. Once microbiologic findings were obtained, the antibiotics administrated were modified according to the results of the microbiological studies and antibiotic susceptibility tests. The duration of treatment was adjusted according to clinical, laboratory, and imaging response to treatment. The removal of the drainage catheter was determined according to the clinical response as well as the volume of drainage output. An intensive follow-up US or CT scan of the liver was performed during hospitalisation and/or subsequent out-patient visits after discharge for each patient in order to evaluate the response to treatment.

Presumed origins of pyogenic liver abscesses were assigned using a modification of the classification by Frey et al. [3]. The origin of the abscesses were determined from available imaging (including US, CT scan with contrast enhancement, and/or ERCP), clinical, pathological and/or surgical information. Pyogenic liver abscesses of biliary origin were defined as those in which clinical features of cholecystitis/cholangitis or documented extrahepatic biliary ductal abnormalities were identified after investigation as was stated above. Pyogenic liver abscesses were considered of cryptogenic origin when no obvious extra-hepatic source of infection could be identified after appropriate investigation. Patient outcomes, including the length of hospital stay, relapse of liver abscess, metastatic infection, the duration to defervesce after admission, and death, were assessed and recorded. Recurrence of liver abscess was defined as initial treatment failure or the development of new clinical and radiological changes consistent with abscess formation subsequent to initial clinical and/or radiographic resolution. All patients were followed up in the outpatient clinic of the hospital after discharge. The median follow-up of patients after discharge was 6 months (range, 4–12 months). Mortality was defined as death during the hospitalisation for a given episode.

Statistical analysis

Statistical analyses were performed with the SAS statistical software, version 8.02 (SAS Institute Inc, Cary, NC, USA). Because of a relatively small sample size in the retrospective study, we performed exact methods for logistic regression instead of conventional logistic regression procedures [20]. We constructed an exact logistic regression model with covariate adjustment to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for associations between dependent and independent variables. For all OR estimates, we considered possible confounding by sex, age, and duration of symptoms prior to admission. Categorical variables were compared between groups with use of the chi-square test or Fisher's exact test (if more than 20% of the expected frequencies were less than 5) as appropriate. For continuous variables, the results were reported as medians with interquartile ranges (IQR) and were compared between groups with use of Mann-Whitney U test. $p < 0.05$ was considered statistically significant in all analyses. All *P* values were two-tailed.

Results

Demography and clinical features

From the 93 patients with a pyogenic liver abscess, 34 were classified into the biliary group and 52 were classified into the cryptogenic group. The remaining 7 patients who were excluded from the analyses had abscesses of another origin (four by haematogenous seeding, one by contiguous spread, one by portal seeding, and one with hepatic cell carcinoma after recent hepatic transcatheter arterial chemoembolisation). The median age at the time of admission was 63.0 years (IQR, 50.8–69.8 years) in the biliary group and 57.5 years (IQR, 44.0–68.8 years) in the cryptogenic group, respectively. There was a male predominance in the biliary (male/female: 19/15) and cryptogenic (male/female: 34/18) groups. The median duration of prodromal symptoms before admission was 4.0 days (IQR, 3.0–7.0 days) in the biliary group and 5.0 days (IQR, 3.0–7.0 days) in the cryptogenic group, respectively. After adjustment for confounders including age, sex, and the duration of prodromal symptoms before admission, biliary stone disorder (cholelithiasis/choledocholithiasis/hepatolithiasis) was more often present in the biliary group than in the cryptogenic group (41% [14/34] *vs* 10% [5/52], respectively; adjusted OR, 5.81; 95% CI, 1.69–24.73; $p = 0.003$). Patients in the biliary group showed more often underlying malignancies compared to patients in the cryptogenic group (18% [6/34] *vs* 2% [1/52], respectively; adjusted OR, 10.66; 95% CI, 1.16–528.30; $p = 0.032$). None of these patients were *human immunodeficiency virus* seropositive. The most common symptoms prior to hospitalisation were fever and/or chills, which were present in 85% (29/34) of patients in the biliary group and in 94% (49/52) of patients in the cryptogenic group respectively. The most frequent sign on admission was body temperature >38.3 °C, which was present in 94% (32/34) of patients in the biliary group and in 87% (45/52) of patients in the cryptogenic group respectively. The frequencies of presenting symptoms/signs did not significantly differ between the two groups after adjustment for confounders ex-

Table 1

Underlying diseases, and clinic features in the biliary and cryptogenic groups.

Variables	biliary N = 34 (%)	cryptogenic N = 52 (%)	biliary vs cryptogenic adjusted OR (95% CI)[d]
Co-existing diseases			
Biliary stone disorder[a]	14 (41)	5 (10)	5.81 (1.69–24.73)
Diabetes mellitus	13 (38)	25 (48)	0.62 (0.22–1.72)
Liver cirrhosis	6 (18)	6 (12)	1.64 (0.38–7.01)
Alcoholism	5 (15)	7 (14)	1.55 (0.33–6.93)
Malignancies	6 (18)	1 (2)	10.66 (1.16–528.30)
Uraemia	3 (9)	5 (10)	0.54 (0.05–3.88)
Symptoms			
Fever/chills	29 (85)	49 (94)	0.52 (0.07–3.34)
Abdominal pain	23 (68)	25 (48)	2.64 (0.93–8.27)
Malaise	19 (56)	20 (39)	1.78 (0.67–4.87)
Anorexia	14 (41)	12 (23)	2.42 (0.80–7.49)
Nausea/vomiting	12 (35)	10 (19)	2.55 (0.78–8.84)
Chest symptoms[b]	11 (32)	15 (29)	1.30 (0.44–3.83)
Weight loss	4 (12)	3 (6)	2.88 (0.37–29.21)
Diarrhea	1 (3)	5 (10)	0.27 (0.01–2.61)
Signs			
Body temperature >38.3 °C	32 (94)	45 (87)	2.45 (0.41–26.55)
RUQ tenderness	21 (62)	26 (50)	1.30 (0.48–3.53)
Murphy's sign[c]	11 (32)	6 (12)	3.67 (1.03–13.86)
Jaundice	12 (35)	15 (29)	1.26 (0.42–3.73)
Shock	6 (18)	8 (15)	1.35 (0.34–5.12)
Hepatomegaly	3 (9)	6 (12)	0.89 (0.13–4.74)
Mental confusion	3 (9)	4 (8)	0.80 (0.07–6.12)
Ascites	1 (3)	2 (4)	0.94 (0.01–19.25)

IQR, interquartile range; RUQ, right upper quadrant; OR, odds ratio; CI, confidence interval.

[a] Biliary stone disorder: including cholelithiasis, choledocholithiasis, or hepatolithiasis.

[b] Chest symptoms: cough, chest pain, and/or short of breath.

[c] Murphy's sign: deep inspiration or cough during subcostal palpation of the RUQ producing increased pain and inspiratory arrest.

[d] The logistic regression model included adjustment for age, sex, and duration of symptoms before admission.

cept that Murphy's sign (deep inspiration or cough during subcostal palpation of the right upper quadrant producing increased pain and inspiratory arrest) was more common in the biliary group compared to the cryptogenic group (32% [11/34] *vs* 12% [6/52], respectively; adjusted OR, 3.67; 95% CI, 1.03–13.86; $p = 0.041$). The co-existing diseases and symptoms/signs on admission of these patients are presented in table 1.

Imaging and laboratory findings on admission

Every patient underwent a radiographic chest and plain abdominal x-ray examination on admission. Abdominal US examinations were performed in all patients and contrast-enhanced CT scan examinations were available in 92% of these patients. Pleural effusion on admission was seen in 68% (23/34) of patients in the biliary group and in 50% (26/52) of patients in the cryptogenic group, respectively. Of the liver abscesses of biliary origin, 22 (65%) were right-sided, 7 (20%) were left-sided, and 5 (15%) were bilateral. Of the liver abscesses of cryptogenic origin, 44 (84%) were located in the right lobe, 4 (8%) were the left lobe, 3 (6%) were in the both lobes, and 1 (2%) was located in caudate lobe. Ninety-one percent (31/34) of liver abscesses of biliary origin and 86% (46/52) of liver abscesses of cryptogenic origin were 10 cm or less in diameter. Multiple abscesses were seen in 13 (38%) patients with pyogenic liver abscesses of biliary origin and in 12 (23%) patients with pyogenic liver abscesses of cryptogenic origin. Gas-forming abscesses were seen in 5 (15%) patients in the biliary group and in 5 (10%) patients in the cryptogenic group. Only one patient who belonged to the biliary group had a ruptured liver abscess on imaging examination. Anaemia (haemoglobin level <14 g/dL in male, or <12 g/dL in female) was the most frequently abnormal laboratory test (31/34, 91%) in the biliary group. Hypoalbuminaemia (serum albumin level <3.5 g/dL) was the most commonly abnormal test (25/30, 83%) in the cryptogenic group. There were no statistical differences in the imaging findings and the abnormality rates of all laboratory measurements between

Table 2

Imaging findings on admission in the biliary and cryptogenic groups.

Variables	biliary N = 34 (%)	cryptogenic N = 52 (%)	biliary vs. cryptogenic adjusted OR (95% CI)[a]
Pleural effusion	23 (68)	26 (50)	1.75 (0.62–5.05)
Location of abscess			
Single lobe	29 (85)	49 (94)	1.00
Both lobes	5 (15)	3 (6)	2.52 (0.45–17.42)
Size of abscess (diameter)			
<5 cm	11 (32)	22 (42)	1.00
5–10 cm	20 (59)	24 (46)	2.07 (0.71–6.52)
>10 cm	3 (9)	6 (12)	0.87 (0.11–5.93)
Number of abscess			
Solitary	21 (62)	40 (77)	1.00
Multiple	13 (38)	12 (23)	1.51 (0.50–4.54)
Gas-forming abscess	5 (15)	5 (10)	1.38 (0.24–7.52)
Rupture of abscess	1 (3)	0 (0)	1.00 (0.03–∞)

OR, odds ratio; CI, confidence interval; ∞, infinity.

[a] The logistic regression model included adjustment for age, sex, and duration of symptoms before admission.

Table 3

Laboratory findings in the biliary and cryptogenic groups.

Parameter	biliary (% abnormality)	cryptogenic (% abnormality)	biliary vs. cryptogenic adjusted OR (95% CI)[a]
WBC count (>10,000/mm^3)	30/34 (88)	36/52 (69)	3.31 (0.86–16.17)
Hb (<14 g/dL in male, <12 g/dL in female)	31/34 (91)	40/52 (76)	2.70 (0.60–17.03)
Serum Alb (<3.5 g/dL)	23/26 (89)	25/30 (83)	0.72 (0.08–6.40)
AST (>40 IU/L)	27/34 (79)	34/51 (67)	1.84 (0.58–6.28)
ALP (>122 IU/L)	21/28 (75)	23/39 (59)	1.79 (0.55–6.24)
TB (>1.3 mg/dL)	19/27 (70)	22/41 (54)	1.91 (0.60–6.51)
BUN (>22 mg/dL)	11/34 (32)	15/51 (29)	0.97 (0.31–.95)
Serum Cr (>1.3 mg/dL)	10/30 (33)	19/51 (37)	0.73 (0.24–2.17)
PT (>13.1 seconds)	5/23 (22)	7/28 (25)	1.05 (0.22–5.14)

WBC, white blood cell; Hb, haemoglobin; Alb, albumin; AST, aspartate aminotransferase; ALP, alkaline phosphatase; TB, total bilirubin; BUN, blood urea nitrogen; Cr, creatinine; PT, prothrombin time; OR, odds ratio; CI, confidence interval.

[a] The logistic regression model included adjustment for age, sex, and duration of symptoms before admission.

the two groups after adjustment for confounders (tables 2 and 3).

Microbiology

Patients of whom blood cultures were obtained, positive rates of bacterial blood cultures were 70% (23/33 patients) with 27 isolates in the biliary group, and 71% (36/51 patients) with 39 isolates in the cryptogenic group, respectively (p = 0.930, employing χ^2 test). Patients of whom abscess cultures were obtained, positive rates of bacterial abscess cultures were 87% (27/31 patients) with 46 isolates in the biliary group, and 98% (49/50 patients) with 52 isolates in the cryptogenic group, respectively (p = 0.068, utilising Fisher's exact test). Patients of whom both blood and abscess cultures were obtained, positive rates of both cultures were 53% (16/30) in the biliary group, and 67% (33/49) in the cryptogenic group, respectively (p = 0.213, employing χ^2 test). Microbiological isolates in the two aetiologic groups are presented in table 4.

Table 4

Microbiologic findings in the biliary and cryptogenic groups.

Organisms	biliary (n = 34)		cryptogenic (n = 52)	
	blood (n = 33)	abscess (n = 31)	blood (n = 51)	abscess (n = 50)
Gram (–) aerobes				
K. pneumoniae	11	16	32	43
E. coli	8	10	3	4
K. oxytoca		1	1	
Pseudomonas aeruginosa	1	2		
M. morganii		1		
Proteus mirabilis		3		1
Enterobacter spp.		1		
Aeromonas spp.		1		
Pantoea spp.			1	
Unidentified gram (–) bacilli	1	1	1	
Gram (+) aerobes				
Enterococcus spp.	2	1		
Streptococcus constellatus		2		
GDS				1
α-haemolytic streptococcus				1
ORSA		1		
CoNS	1		1	
Anaerobes				
B. fragilis	3	3		
Prevotella spp.	1	1		
Fusobacterium spp.		1		
Peptostreptococcus spp.		1		1
Non-spore forming gram (+) anaerobic rods				
Total isolates	27	46	39	52

K. pneumoniae, *Klebsiella pneumoniae; E. coli*, *Escherichia coli; K. oxytoca*, *Klebsiella oxytoca; M. morganii*, *Morganella morganii;* GDS, Group D streptococci; ORSA, oxacillin-resistant *Staphylococcus aureus;* CoNS, coagulase negative Staphylococci; *B. fragilis*, *Bacteroides fragilis.*

With respect to specific pathogens, *K. pneumoniae* were more frequently cultured in patients of the cryptogenic group than in patients of the biliary group after adjustment for confounders (88% [46/52] *vs* 50% [17/34], respectively; adjusted OR, 5.71; 95% CI, 1.68–20.68; p = 0.002). *E. coli* were more frequently cultured in patients of the biliary group than in patients of the cryptogenic group after adjustment for confounders (38% [13/34] *vs* 8% [4/52], respectively; adjusted OR, 5.33; 95% CI, 1.48–25.11; p = 0.010). Similarly, anaerobes were more frequently cultured in patients of the biliary group compared to in patients of the cryptogenic group (21% [7/34] *vs* 2% [1/52], respectively; adjusted OR, 11.46; 95% CI, 1.32–549.3; p = 0.020) (table 5).

Treatment and outcome

All patients received intravenous broad-spectrum antibiotics initially, which included cephalosporins, penicillin derivatives, aminoglycoside and metronidazole. Ninety-four percent (32/34) of patients in the biliary group and 88% (46/52) of patients in the cryptogenic group received two or more antibiotic agents as the initial empirical antibiotic treatment. Three types of initial therapeutic approaches were taken: antibiotics alone, antibiotics plus US-guided PCD, and antibiotics plus image (CT/US)-guided PNA. Antibiotics alone were used in 4 patients with biliary origin and 3 patients with cryptogenic origin. Of 4 patients in the biliary group, 3 patients had an abscess size <2.0 cm in diameter (one with rapid clinical response, one with requirement to subsequent PCD, and one with co-existing uraemia and death of septic shock), and one patient had the abscess size >5 cm in diameter (one with decision against an invasive treatment and death due to uncontrolled sepsis). Of 3 patients in the cryptogenic group, one patient had an abscess size <2 cm in diameter with a rapid clinical response, and 2 patients had an abscess size >5 cm in diameter (one without drainage because of the location and with a benign clinical response, and one with death of septic shock within 24 hours after admission). Drainage by image-guided PNA was performed in 4 patients (4 patients underwent US-guided PNA) in the biliary group and 9 patients (8 patients underwent US-guided PNA and one patient underwent CT-guided PNA) in the cryptogenic group. Drainage by US-guided PCD was performed in 26 patients with biliary origin and 40 patients with cryptogenic origin. In the biliary group, one patient who underwent PCD required subsequent surgical intervention. There was no requirement to change therapeutic modality in all patients in the cryptogenic group. The size of liver abscesses in patients who underwent PNA/PCD was 2 cm or more in diameter except for one patient who underwent CT-guided PNA; the size of the abscess was 1.5 cm in diameter.

The duration of time to defervesce after admission was significantly longer in the biliary group than that in the cryptogenic group (median, 12.0 days *vs* 6.0 days; $p = 0.006$, using the Mann-Whitney U test). After adjustment for confounders, the frequency of time to defervesce >1 week after admission in the biliary group was significantly higher than that in the cryptogenic group (68% [23/34] *vs* 40% [21/52], respectively; adjusted OR, 3.05; 95% CI, 1.09–9.04; $p = 0.030$). The length of hospitalisation was significantly longer in the biliary group than that in the cryptogenic group (median, 20.5 days *vs* 15.0 days; $p = 0.006$, using the Mann-Whitney U test). After adjustment for confounders, there was an increase in the risk of hospital stay >3 weeks among patients in the biliary group compared to patients in the cryptogenic group (47% [16/34] *vs* 15% [8/52]; adjusted OR, 4.34; 95% CI, 1.45–13.91; $p = 0.007$) (table 6). There were no differences in the modality of initial treatment, the duration of time to appropriate antibiotics administration after admission, length of antibiotics administration, and the rates of metastatic infection, recurrence and mortality between the two groups (table 6).

Table 5

Pyogenic liver abscess with regard to specific pathogen in the biliary and cryptogenic groups.

Variable	biliary (%)	cryptogenic (%)	biliary vs. cryptogenic adjusted OR (95% CI)[e]
Bacteremia			
Absent	10/33 (30)	15/51 (29)	1.00
Present	23/33 (70)	36/51 (71)	1.04 (0.35–3.16)
Polymicrobial infection[a]			
Absent	26/34 (76)	49/52 (94)	1.00
Present	8/34 (24)	3/52 (6)	4.10 (0.89–25.91)
K. pneumoniae infection[b]			
Absent	17/34 (50)	6/52 (12)	5.71 (1.68–20.68)
Present	17/34 (50)	46/52 (88)	1.00
E. coli infection[c]			
Absent	21/34 (72)	48/52 (92)	1.00
Present	13/34 (38)	4/52 (8)	5.33 (1.48–25.11)
Anaerobic infection[d]			
Absent	27/34 (79)	51/52 (98)	1.00
Present	7/34 (21)	1/52 (2)	11.46 (1.32–549.3)

OR, odds ratio; CI, confidence interval.
[a] Polymicrobial infection: mixed bacterial flora were cultured in blood and/or abscess cultures.
[b] *K. pneumoniae* infection: *K. pneumoniae* was cultured in blood and/or abscess cultures.
[c] *E. coli* infection: *E. coli* was cultured in blood and/or abscess cultures.
[d] Anaerobic infection: anaerobic isolates were cultured in blood and/or abscess cultures.
[e] The logistic regression model included adjustment for age, sex, and duration of symptoms before admission.

Table 6

Treatment and outcome in the biliary and cryptogenic groups.

Variable	biliary N = 34 (%)	cryptogenic N = 52 (%)	biliary vs. cryptogenic adjusted OR (95% CI)[a]
Initial treatment			
Antibiotics alone	4 (12)	3 (6)	1.00
PNA plus antibiotics	4 (12)	9 (17)	0.43 (0.04–5.09)
PCD plus antibiotics	26 (76)	40 (77)	0.74 (0.25–2.14)
Length of antibiotic treatment > 6 weeks	9 (26)	13 (25)	0.99 (0.30–3.15)
(median; IQR; days)	(33.0; 18.0–44.3)	(31.0; 22.3–42.8)	
Time to defervesce >1 week after admission	23 (68)	21 (40)	3.05 (1.09–9.04)
(median; IQR; days)	(12.0; 4.3–19.5)	(6.0; 3.0–11.0)	
Length of hospital stay >3 weeks	16 (47)	8 (15)	4.34 (1.45–13.91)
(median; IQR; days)	(20.5; 14.0–30.3)	(15.0; 10.3–19.0)	
Metastatic infection	2 (6)	7 (14)	0.42 (0.04–2.49)
Recurrence	4 (12)	1 (2)	5.38 (0.46–277.8)
Death	5 (15)	4 (8)	1.43 (0.24–8.25)

PNA, percutaneous needle aspiration; PCD, percutaneous catheter drainage; IQR, interquartile range; OR, odds ratio; CI, confidence interval.
[a] The logistic regression model included adjustment for age, sex, and duration of symptoms before admission.

Discussion

There were some differences in clinical features of pyogenic liver abscess between the two aetiologic groups, although differentiation of the origin of liver abscesses was very difficult for clinicians based on the host status, presenting symptoms and signs. The underlying co-existing disease might influence the clinical presentation of the individual patient with pyogenic liver abscess. For instance, Murphy's sign was more frequently present in patients with pyogenic liver abscesses of biliary origin, which were often associated with the presence of underlying biliary stone disorder.

Conflicting results have been reported regarding the characteristics of liver abscesses of different origin. Some investigators reported that solitary and multiple abscesses inclined to be cryptogenic and biliary in origin, respectively [13, 16, 21, 22]. However, the result of the present study did not prove that the aetiologic differences between solitary and multiple abscesses were in agreement with the result of Alvarez et al. [23].

Our results confirmed the finding that abscess cultures are more often positive than blood cultures in patients with pyogenic liver abscesses [6, 9, 23–25]. In the two aetiologic groups, the frequencies of positive blood cultures were almost equal, as were those of positive abscess cultures. This is in contrast to previous reports [13, 26] that have emphasised a higher frequency of positive blood cultures in the biliary group and a lower frequency of positive blood cultures in the cryptogenic group. The result of the present study demonstrated a predominance of gram-negative aerobes in both aetiologic groups, especially *K. pneumoniae*. In the present study, *E. coli* were more frequently isolated in the biliary group compared to in the cryptogenic group, concordant with the reports of Cohen et al. [27] and Gyorffy et al. [8]. There was a relatively lower frequency of *K. pneumoniae* isolation in the biliary group compared to that in the other group. The reduction in the frequency of *K. pneumoniae* isolation may be due to an increased frequency of other organism in the biliary group, especially *E. coli*. We found that anaerobic pathogens were more frequently isolated in patients of the biliary group than in patients of the cryptogenic group. This finding implies that initial antibiotics with coverage of anaerobes should be considered especially when the abscess is of biliary origin.

With the advances in imaging techniques, US/CT-guided percutaneous drainage has become a main treatment for patients with pyogenic liver abscesses. The experience from our institution shows that the majority of patients with liver abscesses in both groups were treated with image-guided PCD/PNA for the size of abscess >2 cm in diameter. The mortality rates of patients who underwent PCD/PNA were 10% in the biliary group and 6% in the cryptogenic group respectively. These rates are similar to those of patients on who PCD/PNA was performed with the abscess size >3 cm in diameter [8, 28–31]. Some investigators [32, 33] reported that patients with pyogenic liver abscess treated with antibiotics alone had high frequencies of successful treatment. However, we found high mortality rates in patients treated with antibiotics alone in both groups, in concordance with most of the previous reports [7, 14, 21]. Until the indication for patients treated with antibiotics alone is better defined, the conservative therapeutic modality should be considered only in those patients with small liver abscesses not amenable to PCD/PNA, or in those for whom drainage presents an unacceptable risk. Although some reports [34, 35] advocate open surgical drainage as primary therapy for pyogenic liver abscesses, in our institution surgical intervention is reserved for patients who have failed percutaneous drainage, or those who require surgical management of concurrent intra-abdominal disease This approach is in agreement with most literature [3, 4, 6–10, 13, 14].

In the present study, patients with pyogenic liver abscess in the biliary group had a longer hospital stay and time to defervesce after admission compared to those in the cryptogenic group, despite similar mortality rates of both groups. This likely indicates that the longer time taken for defervescence may be related to co-existing biliary tract infection, rather than to liver abscess per se. Similarly, the longer hospital stay in the biliary group may be related more to the time to correct the underlying biliary abnormality, than to treatment of liver abscess per se. It also seems that different origins of pyogenic liver abscesses should have their own therapeutic strategy. Most literature reports [10, 13–15] suggest that patients with pyogenic liver abscess should be treated with 2- to 3-week parenteral antibiotics and a subsequent 4- to 6-week course of oral antibiotics plus percutaneous needle aspiration, percutaneous catheter drainage or surgical drainage. This approach likely directed the clinicians' decision on the duration of antibiotic administration in this study. This could explain, at least in part, why there were no differences in the duration of antibiotic administration and the modalities of treatment between the aetiologic groups. The optimal duration of antibiotic treatment and the best therapeutic modality for each aetiologic group of patients with pyogenic liver abscess are still undefined, and further prospective experimental studies should be conducted.

In conclusion, this retrospective analysis showed some significant differences between the two groups in terms of underlying malignancy, presence of Murphy's sign, the frequencies of *E. coli*, *K. pneumoniae*, anaerobic pathogen isolation, time to defervesce after admission, and length of hospital stay. Patients in the cryptogenic group have shorter duration of time to defervesce and hospital stay compared to those in the biliary group. The opportunity to discharge early in the cryptogenic group could reduce the costs of therapy and potentially minimise the complications during hospitalisation.

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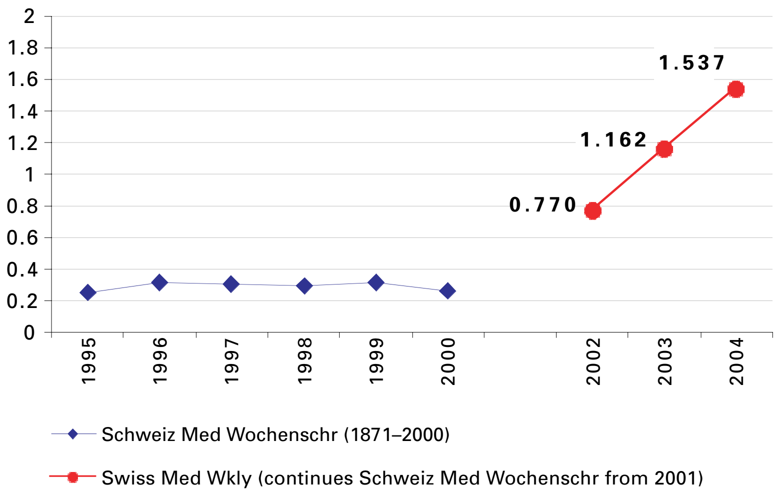

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