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Original Article

Pyogenic liver abscess: clinical profile, microbiological characteristics, and management in a Hong Kong hospital

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Background and Purpose: Pyogenic liver abscess (PLA) is a major hepatobiliary infection with a significant mortality rate of 10% to 25%. Over the past 2 decades, there have been significant developments in the management of this disease. This study describes the demographic, clinical, and microbiological features, management, and poor prognostic factors of PLA in Hong Kong.

Methods: All patients with PLA admitted to the Tuen Mun Hospital, Hong Kong, from July 1998 to June 2004 were included. The medical records of eligible patients were reviewed to obtain demographic, clinical, laboratory, microbiological, and radiological data. Management strategies and factors associated with mortality were studied.

Results: 111 patients were included. Fever, chills, and right upper quadrant pain were the most common presenting symptoms. Low albumin level, elevated alkaline phosphatase, and leukocytosis were the most common laboratory features. *Klebsiella* spp. was the most common etiological agent detected in cultures of blood and abscess aspirates. Fifty two percent of these isolates were *Klebsiella pneumoniae*. Fifty three percent of PLA cases were cryptogenic in origin and 22.5% had underlying biliary pathology. The mortality rate was 11.7%. By multiple logistic regression analysis, hepato-pancreatico-biliary malignancy (p=0.001), requirement for open surgery (p=0.01), and significant delay in diagnosis (p=0.019) were independent risk factors associated with in-hospital mortality.

Conclusion: Although advances in imaging and therapeutic modalities have lead to substantial improvement of outcomes, patients with underlying malignancy and those requiring open surgery in particular are at significant risk of mortality. Delay in diagnosis can result in a fatal outcome. A high index of suspicion with prompt institution of treatment is the cornerstone of successful treatment for patients with PLA.

Key words: Asian continental ancestry group; Etiology; Liver abscess, pyogenic; Treatment outcome

Introduction

Pyogenic liver abscess (PLA) has been recognized since the time of Hippocrates [1]. The condition is still commonly encountered in clinical practice and carries significant morbidity and mortality. The clinical incidence varies from region to region but has been reported to range between 0.006% and 2.2% of hospital admissions [2-7]. The mortality rate for PLA was up to 40% before the 1980s and dropped to 10% to 25% in the recent 2 decades [7-13].

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The etiology and management of PLA has changed substantially in the past few decades. In the first half of last century and prior to the introduction of antibiotics, suppurative appendicitis with portal phlebitis was the most common etiology of this condition [2]. Recently, hepatobiliary causes have replaced portal phlebitis and hematogenous spread as the most common identifiable source of PLA [7-20]. Due to the advent of highly accurate and sophisticated imaging techniques, earlier diagnosis and precise localization of PLA can be achieved. Nowadays, image-guided percutaneous aspiration and drainage of abscess has largely replaced more invasive surgical treatment as the first-line therapy for PLA [21-30]. The aim of this study was to describe the demographic, clinical, and

microbiological features, management, and adverse prognostic factors of PLA in Hong Kong.

Methods

Inpatient medical records with a principal diagnosis of liver abscess (International Classification of Diseases code, 572.0) in Tuen Mun Hospital, Hong Kong, were identified using the Clinical Management System database (Hospital Authority, Hong Kong). The facility is a regional hospital with 1045 acute beds, serving a population of 938,000. From July 1998 to June 2004, 115 consecutive patients with liver abscess were identified. All were adult patients older than 18 years. Three patients with amoebic liver abscesses and 1 patient with fungal liver abscess were excluded from the analysis. The records of the 111 patients with PLA were retrospectively reviewed to determine the demographic characteristics, clinical features, laboratory, microbiological and imaging findings, methods of treatment, and final outcomes.

The following demographic data and clinical information were obtained from each patient's record: age, gender, presenting signs and symptoms, number of non-malignant comorbidities, underlying etiology, diabetes mellitus, presence of malignancy, positive microbiological culture (including blood, abscess aspirate, and bile), imaging modality performed, characteristics of abscess (size, location, and number of abscesses), percutaneous aspiration performed or not, drainage catheter inserted or not, duration of drainage, requirement of surgical treatment, number of days needed to establish diagnosis, and duration of hospital stay.

The following laboratory parameters were retrieved for analysis: hemoglobin level, white cell count, platelet count, urea level, creatinine level, albumin level, globulin level, total bilirubin, alkaline phosphatase (ALP), alanine transaminase (ALT), prothrombin time (PT), and activated partial thromboplastin time (APTT). The value on the day of admission was chosen for analysis.

Search for underlying etiology

The underlying cause of PLA was identified. PLA was considered secondary to benign biliary tract disease in patients with gallstones and a clinical picture of cholecystitis or cholangitis or documented extrahepatic biliary ductal abnormality. PLA was ascribed to be secondary to hematogenous spread when a documented bacteremic episode with another source of infection was found. Portal phlebitis was considered if there was relevant coexisting intra-abdominal infection, such as acute appendicitis or diverticulitis. PLA was determined to be related to hepato-pancreatico-biliary (HPB) malignancy if malignant neoplasm was documented at the same site before or during the investigations for liver abscess or causing biliary obstruction. Cryptogenic abscess was defined as that in which no source of infection could be identified after appropriate investigations.

Management strategies

Diagnosis of PLA was made by a combination of clinical findings, imaging (including ultrasonography [USG] and computed tomography [CT]), and/or aspiration of pus from the lesions. In general, broad-spectrum antibiotics were given intravenously after initial sepsis work-up from blood and/or pus aspiration. Percutaneous needle aspiration of liver abscess was selected if the abscess size was >3 cm in diameter or there was clinical evidence of ongoing sepsis despite antibiotic treatment. The procedure was performed under real-time USG or CT guidance in the radiology department. Needle aspiration was performed using a 22G Chiba needle. The pus was sent for bacterial culture and antibiotic sensitivity testing. This was followed by continuous catheter drainage via an 8 Fr pigtail catheter, unless drainage was not considered beneficial for the patient as determined by the attending radiologist. Surgical drainage was reserved for patients who failed to respond to antibiotics and percutaneous treatment or those who had concurrent intra-abdominal pathology requiring open surgical management. The patients' clinical condition was closely observed and follow-up imaging with USG or CT scan was performed to monitor the progress or resolution of the liver abscess.

Statistical analyses

The data were compiled and analyzed by use of the commercial Statistical Package for the Social Sciences (SPSS) for Windows (Version 10.0; SPSS Chicago, IL, USA). All continuous data were expressed as mean ± standard deviation (SD). Categorical variables were reported as percent. Univariate analysis was performed by chi-squared test to identify significant clinical and laboratory parameters associated with in-hospital mortality. Multivariate analysis by logistic regression was then performed on significant parameters to

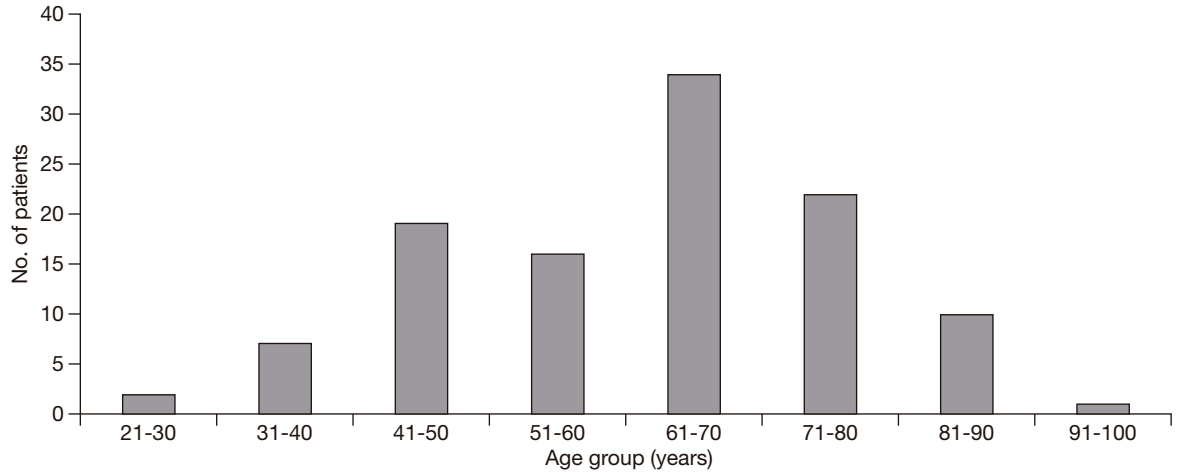

Fig. 1. Age distribution of 111 patients with pyogenic liver abscess.

identify independent prognostic factors of in-hospital mortality. A p value <0.05 was considered statistically significant. Odds ratio and 95% confidence interval were also reported.

Results

Clinical features

From July 1998 to June 2004 inclusive, 111 patients were diagnosed with PLA at Tuen Mun Hospital. All patients were ethnic Chinese. Sixty six patients were men and 45 women (male-to-female ratio, 1.47:1). The mean age was 62.6 years (range, 25 to 92 years). The age group with the greatest number of patients was 61 to 70 years (Fig. 1). The mean duration of symptoms prior to admission was 6.3 days (median, 3 days; range, 1-90 days). As shown in Table 1, the most common presenting features were fever and chills (91%), followed by right upper quadrant pain in 79 patients (71.2%). Comorbidity included hypertension, diabetes mellitus, old stroke, ischemic heart disease, and congestive heart failure. Twenty one patients (18.9%) had diabetes mellitus. Thirty three patients (29.7%) had 2 or more comorbid illnesses (Table 2).

Table 1. Clinical features of 111 patients with pyogenic liver abscess

Symptoms and signs	No. of patients (%)
Fever and chills	101 (91.0)
Right upper quadrant pain	79 (71.2)
Anorexia	18 (16.2)
Septic shock	18 (16.2)
Malaise	15 (13.5)
Jaundice	15 (13.5)
Diarrhea	8 (7.2)
Hepatomegaly	7 (6.3)
Weight loss	5 (4.5)

Laboratory features

The most common laboratory abnormality was low albumin level, which occurred in 103 patients (92.8%). This was followed by leukocytosis in 83 patients (74.8%), increased ALP in 80 patients (72.1%), and elevated ALT in 65 patients (58.6%). Total bilirubin was elevated in 49 patients (44.1%). Notably, 28 patients (25.2%) had a normal white blood cell count and 12 patients (10.8%) had normal total bilirubin and liver enzymes.

Microbiological findings

Blood culture was positive in 47 of 111 patients (42.3%) [Table 3]. Culture from aspirate of liver abscess was positive in 74 of 89 patients who underwent percutaneous aspiration of liver abscess (positive culture rate, 83.1%). Positive bile culture was obtained for 6 patients during endoscopic retrograde cholangiopancreatography (ERCP). The most common organism identified was *Klebsiella* spp. (57.4% of positive blood cultures

Table 2. Number of comorbidities in patients with pyogenic liver abscess

No. of comorbid illnesses	No. of patients (%)
0	35 (31.5)
1	43 (38.7)
2	15 (13.5)
3	8 (7.2)
4	7 (6.3)
5	3 (2.7)

Table 3. Microbiological findings of 111 patients with pyogenic liver abscess

Organism	Blood culture (n = 47) No. (%)	Abscess culture (n = 74) No. (%)	Bile culture (n = 6) No. (%)
Klebsiella spp.	27 (57.4)	37 (50.0)	0
Escherichia coli	6 (12.8)	7 (9.5)	0
Anaerobes	6 (12.8)	6 (8.1)	0
Bacteroides spp.	3 (6.4)	3 (4.1)	-
Peptostreptococcus	1 (2.1)	3 (4.1)	-
Fusobacterium	2 (4.3)	0 (0)	-
Streptococcus milleri	4 (8.5)	2 (2.7)	0
Enterococcus spp.	0 (0)	2 (2.7)	0
Polymicrobial infection	1 (2.1)	14 (18.9)	5 (83.3)
Miscellaneous	3 (6.4)	6 (8.1)	1 (16.7)

and 50.0% of positive abscess cultures; 52.0% of these isolates were *Klebsiella pneumoniae*), followed by *Escherichia coli* (12.8% of positive blood cultures and 9.5% of positive abscess cultures) and anaerobes (12.8% of positive blood cultures and 8.1% of positive abscess cultures). *Streptococcus milleri* accounted for 8.5% of positive blood cultures and 2.7% of positive abscess cultures. Polymicrobials comprised 2.1% of isolates from blood cultures and 18.9% isolates from abscess cultures. The majority of positive cultures from bile were polymicrobials (83.3%). Coagulase-negative *Staphylococcus* was identified in 1 bile culture. There was no statistically significant difference in the presence of underlying diabetes mellitus or metastatic infections in patients with PLA caused by *Klebsiella* spp. versus other etiologic agents.

Radiologic features

USG was the first-line investigation and was performed for 101 patients (91.0%). CT scan was performed for 76 patients (68.5%), being the first-line investigation for 10 patients. Magnetic resonance imaging of the liver was performed for 5 patients (4.5%) to assist diagnosis of liver abscess.

The characteristics of liver abscess found at radiologic imaging are shown in Table 4. The mean size of liver abscess was 6.9 ± 3.0 cm (range, 1-15 cm). The majority of patients had solitary liver abscess (80.2%). Most of the liver abscesses occurred in the right hepatic lobe (n = 75, 67.6%). Thirty patients (27.0%) had liver abscesses in the left hepatic lobe and 6 patients (5.4%) had bilobed liver abscesses. ERCP was performed for 50 patients (45%) to look for a biliary cause of liver abscess. Twenty five patients had abnormal findings, as shown in Table 5. Therapeutic procedures including sphincterotomy, stone extraction or biliary drainage with a plastic stent or nasobiliary drain were needed for 15 patients. A communicating abscess with the biliary tree was found in 2 patients. The procedure was unsuccessful for 6 patients due to difficulty of common bile duct cannulation.

Anatomic disorders of pyogenic liver abscess

Benign biliary tract diseases were identified in 25 patients (22.5%). Two patients (1.8%) had previous choledochojejunostomy. The cause of PLA in 13 patients (11.7%) was assigned to hematogenous origin. The primary sources of sepsis included pneumonia in 5 patients, urinary tract infection in 4 patients, empyema in 2 patients, gallbladder empyema in 1 patient, and palatal abscess in 1 patient. HPB malignancy leading to abscess formation was found in 11 patients (9.9%), including 3 patients with hepatocellular carcinoma (HCC), 3 patients with cholangiocarcinoma, 1 patient with carcinoma of the pancreas and 4 patients had hepatic metastasis (3 from the colon and 1 from the lung). One patient developed liver abscess after transarterial chemoembolization (TACE) for treatment of HCC. No cause could be identified in 59 patients (53%). No patient had documented portal phlebitis

Table 4. Radiologic characteristics of liver abscess

Variable	No. of patients (%)
Size (cm; mean ± SD) [range]	6.9 ± 3.0 (1-15)
No. of abscesses	
1	89 (80.2)
2	13 (11.7)
3	6 (5.4)
4	1 (0.9)
5	2 (1.8)
Type of abscess	
Right lobe	75 (67.6)
Left lobe	30 (27.0)
Bilobed	6 (5.4)

Abbreviation: SD = standard deviation

Table 5. Endoscopic retrograde cholangiopancreatography (ERCP) findings in 50 patients who underwent ERCP

ERCP findings	No. of patients (%)
Normal	19 (38)
Common bile duct stone	11 (22)
Gallstone	4 (8)
Previous choledochojejunostomy	2 (4)
Dilated common bile duct	1 (2)
Common bile duct stricture	1 (2)
Hilar stricture	1 (2)
Intrahepatic duct stone	2 (4)
Intrahepatic duct stricture	1 (2)
Mirrizi's syndrome	1 (2)
Choledochal cyst	1 (2)
Failed cannulation	6 (12)

as the underlying cause. The etiology of PLA in this group is summarized in Fig. 2.

Management and outcome

All patients received intravenous broad-spectrum antibiotics after assessment for sepsis. The mean duration of antibiotic treatment (including intravenous and oral routes) was 30.5 days; this was the only treatment for 22 patients (19.8%). The reasons for not performing image-guided aspiration and drainage was small size of the abscess (<3 cm in diameter) or clinical improvement with antibiotic alone. One patient deteriorated rapidly after admission and died before any percutaneous intervention could be done. Second- and third-generation cephalosporins were the commonest antibiotics used (84.7%), followed by metronidazole (64.0%), and quinolones (18.9%). Aminoglycosides and broad-spectrum penicillins, such as piperacillin-tazobactam, were used for 10.8% and 9.9% of patients, respectively.

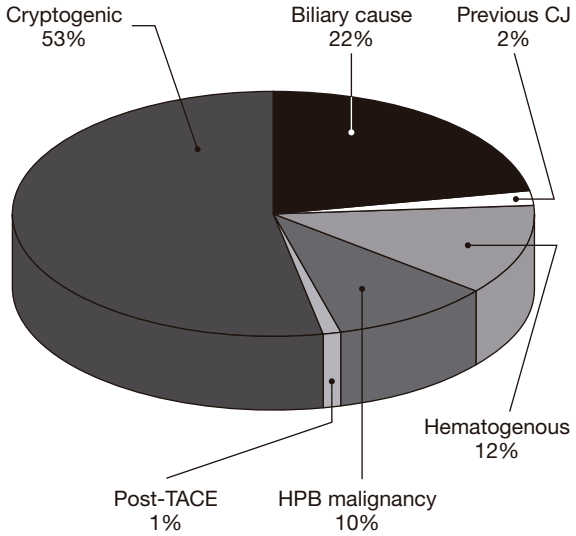

Fig. 2. Anatomic disorders of 111 patients with pyogenic liver abscess. CJ = choledochojejunostomy; HPB = hepato-pancreatico-biliary; TACE = transarterial chemoembolization.

USG-guided needle aspiration of liver abscess was performed in 89 patients (80.2%). Continuous catheter drainage was performed in 76 patients (68.5%). The mean duration of drainage was 13.1 days. A pigtail catheter was not inserted in 13 patients after percutaneous aspiration because the abscess was too solid or it completely collapsed after aspiration. Further drainage by pigtail catheter was not considered beneficial. There was no major complication found after image-guided percutaneous treatment. Surgical drainage was required in 19 patients (17.1%). The main reasons were failure to improve with percutaneous drainage or the patient presenting with acute abdomen requiring emergency laparotomy.

Accurate diagnosis of PLA was achieved at a mean duration of 4.9 days after admission (median, 3.0 days). The mean duration of hospital stay was 30.6 days. Thirteen patients died within the same hospital admission (mortality, 11.7%), and 13 patients (11.7%) required intensive care admission.

Analysis of risk factors

By univariate analysis, 6 factors were found to be significantly associated with hospital mortality, namely:

- duration of symptoms >14 days before presentation;
- >2 comorbid illnesses;
- presence of underlying malignancy;
- >2 abscesses;
- requirement for surgical treatment; and
- diagnosis delayed for >14 days.

When these factors were subjected to multivariate logistic regression analysis, underlying malignancy (p=0.001), requirement for surgical treatment (p=0.01), and delayed diagnosis for >14 days (p=0.019) were independent risk factors associated with mortality.

Discussion

PLA remains a common disease. The incidence is likely to increase because of the ageing population, increasing numbers of immunocompromised patients with chronic illnesses, and increased detection due to advances in imaging techniques. Over the past few decades, we observed significant changes in etiology, diagnosis, bacteriology, treatment, and outcomes of patients.

Before the era of antibiotics, portal phlebitis from a bowel infection was the most common cause of this condition [2]. Since then, the cause of PLA has shifted, first towards biliary tract disorders and more recently towards a cryptogenic origin for most patients [7-20]. In this series, 59 patients (53%) had cryptogenic disease and 25 patients (22.5%) had biliary tract disease, which represented the most common identifiable causes of liver abscess. Hematogenous spread from infection at a distant site was found in 13 patients (11.7%). Portal pyemia could not be demonstrated in any patients. However, 11 patients (9.9%) had underlying HPB malignancy, which became an important cause of liver abscess. Notably, 1 patient developed liver abscess after TACE for HCC. Newer interventional procedures such as TACE and radiofrequency ablation of hepatic tumor are leading to a new generation of patients with PLA. Clinicians who manage patients with HCC should be aware of this condition [31].

There has been a trend for progressive increase in the age of presentation of PLA [2,4,18,20]. This has been attributed to the changing etiology of liver abscess. The mean age of these patients was 62.6 years. Similarly, the most frequent organism isolated from blood and abscess aspirate was *Enterobacteriaceae* (*Klebsiella* spp., followed by *Escherichia coli*). This is probably explained by the high incidence of a biliary cause of liver abscess [7-20]. The mortality rate for liver abscess has fallen considerably over the last few decades [7-13]. Early diagnosis with prompt institution of treatment is the cornerstone of successful therapy. The development of USG and CT scan in the 1970s has revolutionized the diagnosis and treatment of liver abscess. The mortality rate in this series was 11.7%, which is comparable with previous studies [12-16]. Early diagnosis could be established for the majority of these patients. The mean duration from presentation to diagnosis was 4.9 days. However, the presenting features can be non-specific and the diagnosis requires a high index of suspicion. Notably, 10 patients in this study were afebrile and 32 patients did not have typical right upper quadrant pain. Twenty eight patients (25.2%) had normal white blood cell count and 12 patients (10.8%) had normal bilirubin and liver enzymes. Patients with such non-specific clinical features could pose a diagnostic challenge to clinicians.

The most common causative organisms isolated in blood and abscess culture were *Klebsiella* spp., *E. coli*, and anaerobes. Early empirical antibiotics should give adequate coverage for these organisms. Reports from the literature suggest that antibiotics alone, when administered for 4 to 6 weeks, can be curative for a solitary abscess measuring no more than 5 cm in diameter, if a diagnostic aspirate is also employed to ascertain the diagnosis and determine the antimicrobial sensitivity of the cultured microorganism [32]. Intravenous antibiotics were given to all these patients and this was the only treatment for 22 patients (19.8%). The most commonly used antibiotics were second- and third-generation cephalosporins with or without metronidazole. This regimen covered most of the identified organisms and was similar to regimens used in other centers [20,33]. A local guideline had made a recommendation on the choice of appropriate antibiotics to reduce the emergence of bacterial resistance [34]. For patients with community-acquired liver abscess, the preferred regimen for empirical therapy is amoxicillin-clavulanate or ampicillin-sulbactam plus metronidazole to cover the usual bacteria (*Enterobacteriaceae*, *Bacteroides* spp., enterococci) and possible *Entamoeba histolytica*. Cefuroxime plus metronidazole is an alternative choice.

Based on the classic work by Ochsner et al in 1938, open surgical drainage had been the recommended treatment historically [2]. However, such an invasive surgical approach requires general anesthesia and was associated with surgical morbidity and mortality up to 70% in that era. McFadzean et al in Hong Kong reported the first experience of closed aspiration and antibiotic treatment of solitary liver abscess in 1953 [21]. In their series, 14 patients underwent direct aspiration and antibiotics were immediately added to the cavity after irrigation. All patients had uncomplicated recovery. That report was largely ignored until 2 decades later. The advent of modern diagnostic imaging techniques allowed precise localization of the abscess and the development of image-guided percutaneous aspiration and drainage of the abscess in the 1980s [12,35,36]. Nowadays, USG-guided percutaneous intervention is the first-line treatment. PLA is now accepted as a medico-radiologic disease requiring surgical intervention only for correctable offending causes or for failed radiologic evacuation. In this study, percutaneous aspiration of liver abscess was performed in 89 patients (80.2%). Drainage catheters were inserted in 76 patients (68.5%) for a mean duration of 13.1 days. These patients had abscesses that were usually larger than 3 cm in diameter and in locations accessible for percutaneous drainage.

In recent decades, the biliary tree has become the commonest identifiable source of PLA, accounting for 28% to 50% of cases [7-20]. There is also an increasing association with pancreatico-biliary malignancy [6-10,37]. ERCP has been found to be a useful investigation and treatment modality for patients with PLA. In one study, abnormalities were found in 29 of 63 patients [19]. Eight patients underwent endoscopic therapy, including sphincterotomy, stone extraction, and nasobiliary drainage [19]. Another study showed that past history of sphincterotomy was associated with a more rapid resolution of liver abscess [20]. Endoscopic drainage can cure liver abscess for selected patients, such as those with abscesses communicating with the biliary tree [38]. In patients with bile duct stones or stricture, endoscopic therapy can provide biliary drainage and contributes to resolution of these abscesses. Dull et al found that sphincterotomy and local antibiotic lavage via an endoscopically-placed nasobiliary catheter cured 19 of 20 patients with a biliary cause of liver abscess [39]. In this series, 50 patients (45%) underwent ERCP, with intervention needed for 15 patients. Communicating abscess with the biliary tree was found in 2 patients.

A previous study showed that age, rupture at presentation, emergency laparotomy, malignancy, hyperbilirubinemia, and elevated PT were risk factors associated with in-hospital mortality [12]. In the present study, we were able to show that malignancy, requirement for surgical intervention, and delayed diagnosis were independent risk factors associated with in-hospital mortality. There has not been a rising trend in mortality with an increasing age at presentation. This is attributed to advances in diagnosis and treatment of the disease. A recent comparative study between older and younger patients with PLA showed that elderly patients had subtle differences in clinical and laboratory presentations that did not affect the diagnosis, treatment, or mortality [40]. Malignancy has long been described as a poor prognostic factor for patients with PLA, with a mortality rate almost twice as high as for patients without malignant disease [6-10]. The mortality rate is even higher for patients with hepatobiliary malignancy [37]. Poor nutritional status and an immunocompromised state are the likely factors contributing to the poor outcome.

Some limitations of this study should be noted. The retrospective nature of the data may exert a significant influence on the results. The data collected may be affected by factors such as poor standard of record keeping and lack of proper documentation of important events, and can be subject to inter- or intra-observer bias during case review. The results represent the experience from a single centre, and may not be generalizable to other areas with different epidemiologic or clinical settings.

Although patients with PLA continue to experience significant morbidity and mortality, the prognosis is much improved with the availability of broad-spectrum antibiotics, minimally invasive percutaneous treatment and, more recently, laparoscopic surgery. Delay in diagnosis, need for open surgical treatment, and malignancy represent the most important risk factors associated with mortality. With further development of imaging techniques and new treatment modalities, we hope that the outcome of patients with PLA can be further improved.

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