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Factors associated with treatment failure of percutaneous catheter drainage for pyogenic liver abscess in patients with hepatobiliary-pancreatic cancer

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Abstract

BACKGROUND: The aim of this study was to identify predictors of treatment failure of percutaneous catheter drainage (PCD) in patients with hepatobiliary-pancreatic cancer with pyogenic liver abscess (PLA).

METHODS: Medical records of 44 patients with PLA with underlying hepatobiliary-pancreatic cancer who underwent PCD under computed tomographic guidance as primary treatment between January 2001 and December 2010 were collected and reviewed. Included patients were diagnosed with cholangiocarcinoma (n = 16), hepatocellular carcinoma (n = 12), pancreatic carcinoma (n = 9), carcinoma of the ampulla of Vater (n = 6), and gallbladder cancer (n = 1). The clinical factors related to failure of PCD were determined using logistic regression.

RESULTS: The median age of the 44 patients with PLA was 68 years, and 48% were men. PCD failed in 15 patients (34%). Of the 15 patients with PCD failure, 12 subsequently required surgical intervention because of either clinical deterioration or imaging that demonstrated failure of abscess resolution with PCD. Three of these patients died with the initial drain in place before resolution of the abscess. In patients requiring surgery after PCD failure, the frequency of cure or abscess resolution reached 67%. Fourteen patients (32%) died during hospitalization. Multivariate analysis identified that multiloculated abscesses ($P = .005$) and abscesses with biliary communication ($P = .036$) were associated with failure of PCD.

CONCLUSIONS: Multiloculated abscesses and lesions with biliary communication pose a greater likelihood of failure of PCD in patients with hepatobiliary-pancreatic cancer with PLA. Early surgical intervention after PCD failure should be considered for these patients.

Dr Y.-T. Lee made an equal contribution to this work as the second author. Dr C.-C. Chen made an equal contribution to this work as the first author.

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Pyogenic liver abscess (PLA) is an infrequent but potentially life-threatening illness, accounting for 2 to 45 cases per 100,000 hospital admissions each year.[1–5] Currently, treatment of PLA typically relies on antibiotics and image-guided intervention. Percutaneous catheter drainage (PCD) under image guidance has evolved over the past 2 decades and is currently the primary treatment for PLA,[1,2,5–11] although some still advocate either surgical intervention or percutaneous needle aspiration.[12,13] Several attempts to identify risk factors for treatment failures of PCD for PLA have been conducted.[13–16] The presence of multiple abscesses, multiloculated abscesses, abscess > 5 cm in diameter, and abscesses communicating with the biliary system reportedly increase the risk for failure for PCD and may warrant an early surgical intervention; however, this issue remains debatable in the literature.[13–16] These studies generally reported on PLA related to benign disease, whereas malignant disorders are often associated with adverse outcomes. Hepatobiliary-pancreatic malignant disorder has been reported to carry a greater serious prognosis of PLA than non-hepatobiliary-pancreatic cancer.[17] The therapeutic effectiveness of image-guided PCD for patients with PLA with underlying hepatobiliary-pancreatic cancer has seldom been thoroughly investigated. Improved understanding of the clinicopathologic factors contributing to treatment failure of PCD in patients with PLA with hepatobiliary-pancreatic cancer is needed. The purpose of this retrospective study was to collect detailed clinical information, including clinical manifestations, imaging, laboratory findings, microbiologic studies, treatment, and outcomes, to identify factors contributing to PCD failure in patients with PLA with underlying hepatobiliary-pancreatic cancer.

Methods

Subjects

Medical records of patients aged > 18 years who had been discharged between January 2001 and December 2010 with diagnoses of PLA from China Medical University Hospital were reviewed. PLA was defined on the basis of the following conditions: (1) evidence of ≥1 discrete abscess cavity of the liver from imaging studies (ie, abdominal ultrasonography and/or computed tomography [CT] with contrast enhancement) and (2) positive bacterial blood or abscess culture results. In total, 463 patients with PLA were admitted to the hospital during this period, and 47 patients with PLA had histopathologically confirmed diagnoses of malignancy originating from the hepatobiliary-pancreatic system. Initial surgical treatment of PLA was not indicated except in patients with an initial presentation with intraperitoneal rupture. Of those 47 patients, 3 patients (1 treated with antibiotics alone, 1 who had an initial presentation with abscess rupture receiving only antibiotic therapy because of refusal to undergo initial surgery and at the same time was transferred to other medical center based on the patient's own will, and 1 undergoing percutaneous needle aspiration as primary treatment) were excluded from analysis. The remaining 44 patients underwent initial CT-guided PCD (using an 8Fr to 10Fr catheter), performed by a well-trained and licensed radiologist using the modified Seldinger technique, and were included in this study. Of these, 16 patients had cholangiocarcinoma, 12 had hepatocellular carcinoma, 9 had pancreatic carcinoma, 6 had carcinoma of the ampulla of Vater, and 1 had gallbladder cancer. This study was approved by the research ethics committee of the institute.

Variable definition and data collection

Demographic data, clinical presentation, clinical course, laboratory, microbiologic, and imaging findings, treatment, and outcomes were reviewed and analyzed. Gram stain, bacterial cultures (standard aerobic and anaerobic diagnostic methods), and tests for antimicrobial susceptibility were conducted in all patients.[18] *Escherichia coli* infection, *Klebsiella pneumoniae* infection, anaerobic infection, or polymicrobial infection were considered in the presence of *E coli*, *K pneumoniae*, anaerobic isolates, or mixed bacterial flora in blood and/or abscess cultures. Abscesses were considered cryptogenic in origin when no causative lesions were demonstrated. A diagnosis of multiple abscesses was made when the presence of normal intervening liver parenchyma was separating multiple abscesses and/or there was evidence that the abscesses were in different segments of the liver. Multiloculated abscess were diagnosed by the presence of enhancing internal septations on contrast-enhanced CT. Abscess communicating with the intrahepatic biliary tree system was defined as the presence of bilious fluid within the collection bag or the presence of pneumobilia on CT and a subsequent demonstration of endoscopic retrograde cholangiopancreatography or percutaneous transhepatic cholangiography with contrast study showing communication of the abscess cavity with the biliary tree system. The imaging results were assessed and reviewed by an experienced and licensed radiologist. Initial empiric broad-spectrum antibiotics were administered intravenously after blood and/or liver abscess specimens had been obtained. Antibiotics were subsequently tailored, if necessary, on the basis of the culture and sensitivity results. A multi-drug-resistant isolate was defined as any pathogen resistant to ≥3 of the antibiotic classes. Metastatic infection was defined when extrahepatobiliary infectious foci were found in patients who had undergone treatment for liver abscess and when bacterial strains isolated from the extrahepatobiliary foci were the same as those that had been isolated from the abscess culture.[19,20] Failure of PCD was defined as requiring surgical intervention or death while abscess drains were in place. The indications for drain removal were (1) no signs of infection (ie, pyrexia, leukocytosis, and negative culture results) and drainage was nonbilious, and (2) the output was <5 to 10 mL/d for 24 to 48 hours. Recurrence of liver abscess was defined as the development of new clinical and

Table 1 Demographic data, clinical features, and concomitant diseases in 44 patients with hepatobiliary-pancreatic cancer with PLA undergoing PCD

Variable	All patients (n = 44)	Patients with PCD failure (n = 15)	Patients without PCD failure (n = 29)	*P*
Men	21 (48%)	7 (47%)	14 (48%)	.919
Age (y)	68 (63–78)	76 (71–78)	63 (61–77)	.061
Metastasis	15 (34%)	7 (47%)*	8 (28%)†	.206
Origin of abscess				.111
Biliary	42 (96%)	13 (87%)	29 (100%)	
Others	2 (4%)	2 (13%)	0	
Comorbidities				
Diabetes mellitus	14 (32%)	6 (40%)	8 (28%)	.501
Biliary disorders‡	20 (46%)	5 (33%)	15 (52%)	.246
Liver cirrhosis	9 (21%)	4 (27%)	5 (17%)	.464
Interval between symptoms before admission and diagnosis after admission (d)	3 (2–7)	3 (2–7)	3 (2–9)	.365
Symptoms or signs on admission				
Body temperature > 38.3°C	36 (82%)	10 (67%)	26 (90%)	.099
Jaundice	28 (64%)	12 (80%)	16 (55%)	.105
Abdominal pain or tenderness	26 (59%)	10 (67%)	16 (55%)	.462
Malaise	24 (55%)	9 (60%)	15 (52%)	.601
Blood pressure < 90/60 mm Hg	12 (27%)	5 (33%)	7 (24%)	.722

Data are expressed as number (percentage) or as median (interquartile range).
*Including 6 with lymph node metastasis and 1 with pancreatic metastasis.
†Including 8 with lymph node metastasis.
‡Including biliary stone diseases and prior hepatobiliary surgery.

radiologic changes after clinical and/or radiologic resolution. Surgical intervention was required when patients demonstrated either deterioration or no improvement in clinical symptoms or signs, persistent abscesses, or abscess rupture after initial treatment with PCD despite multiple drainage endeavors. Response to treatment was evaluated in each patient by a series of follow-up abdominal ultrasound or computed tomographic scans of the liver either during hospitalization and/or at the time of subsequent office visits postdischarge. Case fatality was defined as death during hospitalization for PLA.

Statistical analysis

Comparisons between groups for continuous variables were made using Mann-Whitney *U* tests. Categorical variables were compared between groups using either χ^2 or Fisher's exact tests (if the expected value of $\geq$1 cell was $<$5). The relationships between demographics, clinical features, laboratory results, and therapeutic variables and failure of PCD were analyzed. Significant variables on univariate analyses were subject to logistic regression using a forward method to identify significant independent risk factors for failure of PCD. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated in the logistic regression model. All statistical tests were 2 tailed, with *P* values $<$ .05 denoting statistical significance. All analyses were performed using SAS version 8.2 (SAS Institute Inc, Cary, NC).

Results

Demographic and clinical characteristics

The median age of the 44 PLA patients with hepatobiliary-pancreatic cancer was 68 years. Forty-eight percent were men, and 34% had lymph node or other organ involvement. The most common origin of liver abscess had a biliary etiology (suppurative cholangitis or acute cholecystitis; 96%). One patient with hepatocellular carcinoma underwent transcatheter arterial embolization 8 weeks before admission. No source of the abscess could be determined in 1 patient despite thorough investigation. During hospitalization, 29 patients (66%) were successfully treated with PCD, and the other 15 patients failed to respond after the initial PCD. There were no differences in demographic data, origin of abscess, concomitant disorders, and clinical features between patients who did or did not respond to PCD (Table 1).

E coli (71%) was the most commonly aerobic isolate, followed by *K pneumoniae* (27%). The recovery frequency of blood culture was 71% in 42 patients who had blood cultures. Neither microbiologic nor laboratory findings were significantly different between patients with and without PCD failure. Communication with the biliary tract was diagnosed via contrast study and was noted in 9 patients (21%). Of these, 8 patients had concomitant biliary tract obstruction. All 8 of these patients underwent treatment

Table 2 Bacterial, laboratory, and imaging findings in 44 patients with hepatobiliary-pancreatic cancer with PLA undergoing PCD

Variable	All patients (n = 44)	Patients with PCD failure (n = 15)	Patients without PCD failure (n = 29)	*P*
Microbiologic characteristics				
Anaerobic infection	8 (18%)	2 (13%)	6 (21%)	.695
Polymicrobial infection	27 (61%)	8 (53%)	19 (66%)	.431
Multi-drug-resistant isolates	28 (64%)	10 (67%)	18 (62%)	.764
Imaging findings				
Multiple abscesses	14 (32%)	8 (53%)	6 (21%)	.042
Gas-forming abscess	6 (14%)	0	6 (21%)	.080
Right lobar involvement	33 (75%)	9 (60%)	24 (83%)	.144
Abscess > 5 cm in diameter	31 (71%)	11 (73%)	20 (69%)	1.000
Multiloculated abscess	14 (32%)	10 (67%)	4 (14%)	.001
Abscess with biliary communication	9 (21%)	6 (40%)	3 (10%)	.044
Pleural effusion	21 (48%)	5 (33%)	16 (55%)	.169

with either percutaneous or endoscopic drainage for the biliary obstruction.

Patients with PCD failure were more likely to have either multiple abscesses ($P = .042$) or multiloculated abscesses ($P = .001$) and the occurrence of abscess with biliary communication ($P = .044$) compared with those without PCD failure (Table 2). Other imaging characteristics did not appear to differ between the 2 groups.

Treatment and patient outcomes

All patients received parenteral antibiotics, including cephalosporins, penicillin, and/or aminoglycosides. The choice of antibiotics was based on the preference of the clinician in charge, the condition of the patient, and the culture and antimicrobial sensitivity data. Thirty-five patients (80%) received either second-generation or third-generation cephalosporins with or without gentamicin. There was no difference in antibiotic treatment between patients with and without PCD failure. Twenty-eight patients with biliary obstruction required biliary drainage via either endoscopic retrograde cholangiopancreatography or percutaneous transhepatic cholangiography. No metastatic infection occurred in any patient.

Fourteen patients (32%) died during hospitalization. In the group of patients who were successfully treated with PCD, 4 died because of progression of malignancy, and 1 died of pneumonia. Among the 15 patients with PCD failure, 12 subsequently required surgical intervention because of either clinical deterioration or imaging results demonstrating abscess rupture or failure of abscess resolution with PCD. Of the 12 with surgery, 7 had abscess drains in place, 3 died of uncontrolled sepsis, and 2 died of liver failure or progression of malignancy; the frequency of cure or abscess resolution was 67% (8 of 12) in patients requiring surgery after PCD failure (Appendix 1 of the supplementary data). The remaining 3 patients without surgery died before resolution of the abscess. The median hospital stay in all 44 patients was 26 days (interquartile range, 19–38 days). The median follow-up duration of 30 patients after discharge was 3.6 weeks (interquartile range, 2.7–6.1 weeks). There were no differences in the duration of antibiotic treatment, length of hospital stay, abscess recurrence, and time to defervesce after admission between the groups of patients who did or did not respond to PCD, but the group of patients who failed to respond to PCD had a higher case fatality rate than patients who were successfully treated (60% vs 17%, $P = .007$). Treatment and outcomes are summarized in Table 3.

Risk factors for failure of PCD

Significant clinical variables obtained from univariate analyses (shown in Tables 1 and 2) were subjected to multivariate analysis. Three variables fit the logistic regression model: multiloculated abscess (OR, 12.1; 95% CI, 2.2–67.2; $P = .005$), abscess with biliary communication (OR, 8.7; 95% CI, 1.2–65.1; $P = .036$), and multiple abscesses (OR, 4.1; 95% CI, .7–23.3; $P = .108$). Ten patients had multiloculated abscess in the PCD failure group. Nine of these patients required subsequent surgical interventions, but 3 survived and 6 died of uncontrolled sepsis, liver failure, or progression of malignancy. Six patients had abscesses with biliary communication in the PCD failure group. Four of these patients required additional surgical interventions and eventually survived. The remaining 2 (1 with subsequent surgical drainage and 1 with PCD) died of overwhelming sepsis while the drains were still in place.

Comments

Image-guided PCD for PLA has been reported to have a low failure rate. In the general adult population, failure rates have ranged from 0% to 34% over the past 15

Table 3 Treatment and outcomes for 44 patients with hepatobiliary-pancreatic cancer with PLA

Variable	All patients (n = 44)	Patients with PCD failure (n = 15)	Patients without PCD failure (n = 29)	*P*
Antibiotic modality				.838
Penicillin group ± aminoglycoside	9 (20%)	3 (20%)	6 (21%)	
Second-generation cephalosporin ± aminoglycoside	17 (39%)	5 (33%)	12 (41%)	
Third-generation cephalosporin ± aminoglycoside	18 (41%)	7 (47%)	11 (38%)	
Duration of intravenous antibiotics (d)	19 (13–33)	22 (12–42)	18 (14–29)	.302
Duration of total (intravenous + oral) antibiotics (d)	28 (17–43)	24 (22–48)	32 (17–43)	.700
Percutaneous or endoscopic biliary drainage	28 (64%)	9 (60%)	19 (66%)	.718
Duration of PCD (d)	14 (11–24)	12 (10–20)	14 (12–25)	.304
Time to defervesce after admission (d)	6 (2–20)	18 (0–25)	5 (2–8)	.052
Recurrence	2 (5%)	2 (13%)	0	.111
Hospital stay (d)	26 (19–38)	33 (24–51)	26 (18–37)	.378
Fatality	14 (32%)	9 (60%)	5 (17%)	.007

Data are expressed as number (percentage) or as median (interquartile range).

years.[1,13,16,21,22] In the present study, the treatment failure rate was 34% of patients with PLA with underlying hepatobiliary-pancreatic cancer who underwent CT-guided PCD, which was comparable with the aforementioned reports. In patients requiring surgical intervention after PCD failure, the frequency of disease remission reached 67%, a finding similar to that of Mezhir et al,[22] with a cure rate of 60%. Furthermore, patients with multiloculated liver abscesses and lesions communicating with the biliary system were at risk for treatment failure of PCD as an initial treatment modality in patients with PLA with underlying hepatobiliary-pancreatic cancer.

With ongoing improvement in diagnostic imaging studies, PLA with multiloculation has been increasingly noted. Farges et al[23] and Barakate et al[24] reported that patients with multiloculated PLAs had higher mortality and lower success rates in patients treated with PCD compared with those with uniloculated PLAs, which agrees with the present study. In contrast, Liu et al[16] did not report a similar finding. This disparity could be attributed to variations in the study populations. The mechanism of multiloculated abscesses has not been fully clarified, but several hypotheses exist. For example, some researchers suggest that it involves a coalescent process from clustering abscesses, ultimately forming a larger abscess in which the septal components can be broken and liquefied, and the clustering abscesses communicate with one another.[25,26] Alternatively, multiple small locules aggregate and communicate with one another.[27,28] Liu et al noted that multiloculated abscesses can be drained by maneuvering a guide wire to the abscess cavity and rotating the wire to destroying the septae, thereby eliminating the need for surgical treatment. In our opinion, more evidence is needed to support this contention. Tan et al[13] suggested that surgical intervention as the initial modality for treatment of multiloculated liver abscesses had a favorable result, with less treatment failure, less need for secondary procedures, and shorter hospitalization than patients undergoing PCD. Moreover, the PCD failure rate of 71% in patients with multiloculated abscesses herein was higher than in general adults with multiloculated liver abscesses, which ranges from 0% to 33%.[13,16,21] Thus, early surgical intervention after PCD failure seems to be a reasonable choice for this kind of patients, but further prospective studies are needed to confirm this observation.

In the present study, PLA with biliary communication was a factor associated with treatment failure after PCD, as previously reported.[15,16,22] Biliary communication leading to continuous output of bile into the abscess cavity via a communicating tract could preclude the tract from closing and healing. Two previous studies revealed that patients with PLA with biliary communication (but no obstruction) had a higher cure rate after PCD than those with biliary communication and obstruction.[29,30] In the present study, only 1 of the patients with a biliary communication did not have a biliary obstruction; therefore, it is not possible to make a similar conclusion, despite a higher cure rate of PCD in patients with biliary communication but no obstruction, because of a small number of cases with biliary communication. In contrast, although only 2 patients were completely cured with initial PCD among the 8 patients with biliary communication and obstruction who had undergone biliary draining for biliary decompression, the total eventual cure rate of biliary draining for biliary communication with or without obstruction was 78% when 6 patients having subsequent surgery after PCD failure were included, a finding in concordance with the observations of Sugiyama and Atomi,[15] which indicates that biliary drainage can be beneficial in patients with PLA with biliary communication because biliary drainage or stenting may result in biliary decompression by obliterating the pressure gradient between the biliary tract and the duodenum, and thereby helping abscess resolution.

It should be acknowledged that this study was limited by its retrospective design. The data were limited to what had

been recorded in the medical records, which may inevitably lead to insufficient information. Nonetheless, this study included a relatively large number of patients with PLA with underlying hepatobiliary-pancreatic cancer, focusing on factors related to PCD failure.

Conclusions

Patients with PLA with underlying hepatobiliary-pancreatic cancer had an acceptable PCD success rate. Moreover, the presence of multiloculated liver abscesses and lesions communicating with the biliary system increased the likelihood of PCD failure for patients with hepatobiliary-pancreatic cancer with PLA. In addition to abscess drainage, biliary drainage would be imperative for patients with PLA who have biliary tract communication with or without biliary obstruction. Surgical intervention should be considered when clinically indicated and in those with PCD failure, especially for patients with PLA with multiloculated abscesses or biliary communications.

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Supplementary Data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.amjsurg.2012.03.006.

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