Pyogenic Liver Abscess

Diagnostic and Therapeutic Strategies

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A retrospective review of 26 adult patients admitted to University of California, Davis, Medical Center (UCDMC) with pyogenic liver abscess (1980–1986) was performed to ascertain the impact of rapid diagnosis and percutaneous drainage. Ultrasonographic examinations and computed tomography (CT) scans were highly sensitive and noninvasive imaging modalities. Sixteen patients had solitary abscesses and seven had multiple microscopic abscesses. The median time interval from admission to diagnosis and therapy was 2 and 3 days, respectively. Origin of the abscess was determined in 22 patients, the biliary tree being the most common source. Medical therapy was successful in three patients with microabscesses but failed in two. Nine patients had percutaneous drainage; two required repetitive percutaneous catheter placement, and two proceeded to surgical drainage. Twelve patients had surgical drainage; one required repetitive surgical drainage. Postdrainage complications were minimal in all groups. Overall mortality role was 11.5% (two patients). Deaths were related to delay in diagnosis, gram-negative sepsis at presentation, and biliary origin of the abscess.

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RECENT REPORTS have emphasized the changing epidemiology, treatment, and prognosis of pyogenic liver abscess.[1-6] The availability of imaging modalities, ultrasonography, and computerized tomography (CT) and the successful application of closed percutaneous drainage of pyogenic liver abscess have changed approaches to diagnosis and therapy. We report our 6-year experience with pyogenic liver abscess with emphasis on diagnostic and therapeutic strategies.

Patients and Materials

Between January 1, 1980, and June 30, 1986, 26 patients older than the age of 16 years of age were admitted to University of California, Davis, Medical Center (UCDMC) with a final diagnosis of pyogenic liver abscess confirmed microbiologically and/or pathologically. UCDMC is a 453-bed University-based teaching hospital. Pediatric patients (N = 4) with pyogenic liver abscess and adult patients with amebic liver abscess (N = 14) identified during this time period were excluded from analysis. The case records of these 26 patients were reviewed with particular care devoted to ascertaining clinical features, time interval to diagnosis and therapy, imaging studies, microbiology, initial treatment, necessity for retreatment, and outcome.

Results

Clinical and Laboratory Features

Nineteen patients were men and seven were women. Their ages ranged from 21 to 76 years, with a mean of 47. Six patients were referred from other institutions. APACHE II scores, a physiologic measure of the severity of illness, ranged from 0 to 33, with a mean of 9.3.[7] More common signs and symptoms are shown in Table 1, and initial laboratory findings are shown in Table 2. Fourteen of the 26 patients had one or more co-morbid factors (biliary disease, malignancy, drug-related immunosuppression, diabetes mellitus, recent abdominal surgery, or chronic alcoholism). The initial chest roentgenogram abnormalities included atelectasis, hemidiaphragmatic elevation, or pleural effusion at the right base in 13 patients.

Diagnosis

Twenty-five of the 26 patients were diagnosed before death. The median number of days the patients had symptoms before hospitalization was 14 (range: 1–120 days). In six patients the diagnosis was made before hos-

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TABLE 1. *Clinical Features (N = 26)*

	No.	(%)
Symptoms		
Fever	23	(88)
Nausea/malaise	18	(69)
Weight loss	15	(58)
Abdominal pain	10	(38)
Signs		
Fever	25	(96)
RUQ tenderness	16	(62)
Hepatomegally	10	(38)
Jaundice	3	(12)

pitalization. In the remaining patients, the most common types of tentative diagnoses and symptoms cited on admission were cholecystitis, fever and abdominal pain, and sepsis of unknown source. Diagnosis was usually made after ultrasonography or CT scan for evaluation of abnormal liver enzymes, right upper quadrant tenderness, or chest roentgenographic abnormalities. Median length of patient hospital stay before a diagnosis was established was 2 days (range: 0–8 days). Thirteen patients had diagnostic aspiration or drainage before definitive therapy. Purulent material was aspirated in all patients, and there were two complications (one ruptured abscess necessitating immediate surgery and one hemorrhage necessitating transfusion).

Noninvasive Imaging

The initial imaging study is shown in Table 3. Ultrasonographic examination performed in 17 patients and the findings were positive in 15. In one patient a single abscess was missed and in another the ultrasonographic examination showed a single abscess in a patient with multiple abscesses. Both of these patients had nonhomogeneous liver scans secondary to co-existing liver disease. The initial procedure was CT scan for six patients and sulfur colloid scanning in two patients. There were no false-negative results in either group. One patient had an exploratory laparotomy that had normal findings. After operation an ultrasonographic examination was performed that indicated an abscess.

Most patients had multiple imaging studies during therapy. Both ultrasonographic examination and CT scan were highly specific, and we found little difference in terms of information obtained from the two modalities when used in follow-up examinations.

Abscess Characteristics

Three patients had multiple microabscesses (less than 1.5 cm), all of whom had a clinical picture of ascending cholangitis. Sixteen patients had solitary liver abscess, and seven patients had multiple abscesses (29 macroscopic abscesses in 23 patients). Twenty-three of the 29 macroabscesses were located in the right lobe. Eleven abscesses were between 1.5 and 5 cm, 12 abscesses between 5 and 8.0 cm, and six abscesses were greater than 8.0 cm. Twelve of 29 abscesses appeared loculated by ultrasonographic examination or CT scan, although these loculations were confirmed at subsequent drainage in only two patients.

Microbiology

All 26 patients had positive abscess culture results despite that they had received broad-spectrum antibiotics at the time of the initial culture of the liver abscess (Table 4). A total of 56 different organisms were isolated in 26 patients. Eight patients (31%) had monomicrobial cultures. Two organisms were isolated in 10 patients, three organisms in five patients, four organisms in two patients, and five organisms in one patient. As expected, the bacteriologic study showed a predominance of gram-negative aerobes (22 of 56) and anaerobes (27 of 56). Blood culture results were positive in nine of the 19 patients from which they were obtained.

Origin of Pyogenic Abscess

The origin of the pyogenic liver abscess was eventually determined in 22 (85%) patients (Table 5). In 14 patients the source was evident at diagnosis and was known before therapy was initiated. Clinical history and ultrasonographic or CT imaging were most helpful in determining origin, especially as it pertained to the biliary tree. In the remaining 12 patients the source was not evident at the time of therapy but was determined in

TABLE 2. *Laboratory Findings*

	Mean	Range	Percentage	Abnormal
Hemoglobin (g/L)	11.8	8.0–15.4	62	(<12 g/L)
Leukocyte count (per mm^3)	16,600	7,00–31,000	73	(>10,000/mm^3)
Alkaline phosphatase (IU/L)	462	77–3774	73	(>115 IU/L)
GGTP (IU/L)	236	15–1500	73	(100 IU/L)
Albumin (g/dL)	3.0	1.4–4.6	69	(<3.5 g/dL)
Bilirubin (mg/dL)	1.98	0.2–13.7	23	(>1.4 mg/dL)
Serum glutamic oxaloacetic transaminase (IU/dL)	83.5	19–580	31	(>40 IU/dL)

TABLE 3. *Initial Imaging Study*

	No.	(%)	Positive Results	Negative Results
Ultrasound	17	(65)	15	2
Computed tomography	6	(23)	6	0
Scintiscan	2	(8)	2	0
Laparotomy	1	(4)	0	1

* Percentage of total number.

eight patients during the course of therapy. A barium enema was performed in six patients, which showed recent evidence of perforated diverticulum in two patients and extensive diverticular disease in another. Endoscopic retrograde cholangiopancreaticography was performed in four patients and had normal findings in all cases. The origin could be determined at laparotomy in three patients, with further clinical evaluation in one patient, and at necropsy in an additional patient.

Nine liver abscesses (35%) originated in the biliary tree, seven from cholecystitis and/or cholangitis and two from malignant obstruction of the biliary tree. Of the five cases originating from the colon, the origin was only evident in two patients on admission. Local penetrating trauma accounted for three cases and seeding from a source of infection in a distant location in three other patients. No source could be determined in four patients, despite a thorough investigation.

Therapy and Outcome

All patients generally received broad-spectrum antibiotics before diagnosis. The median time from admission to initiation of antibiotic therapy was 1 day (range: 0–8 days). The median time from admission to a drainage procedure was 3 days (range: 1–8 days). The initial treatment and requirement for retreatment for the 26 patients are shown in Table 6. In one patient, a diagnosis of liver abscess was not made before death. The patient received continuous antibiotics as the sole treatment, and an abscess was discovered at necropsy. One patient had a single aspiration followed by antibiotics. The abscess re-accumulated and was successfully treated by closed continuous percutaneous drainage.

Nine patients, three of whom had multiple abscesses, were initially treated by closed, continuous percutaneous drainage. All were clinically and hemodynamically stable. Diagnostic aspiration was followed by placement of a 7–12 Fr pigtail catheter by use of a modified Seldinger technique.[8] Catheter placement was carried out under guidance with either ultrasonography or CT scan. Once the catheter was adequately positioned, saline irrigation was performed and the drains were placed to gravity drainage. One drain was placed per abscess cavity. Patients were monitored by CT scan or ultrasonography to ensure complete drainage. The drains were left in for an average of 8 days (range: 4–18 days) and removed when the abscess cavity had collapsed around the catheter. Percutaneous drainage was considered to have failed if any of the following were noted: (1) complications related to catheter insertion that necessitated surgical intervention; (2) lack of improvement or worsening condition after 72 hours of percutaneous drainage; and (3) recurrence of the abscess within 3 months of therapy. Four patients' percutaneous drainage failed (Fig. 1). Two of these were treated successfully by placement of a second percutaneous catheter, and one patient went directly to successful surgical drainage. A blood clot was found in the abscess cavity. Another patient had successful surgical drainage after failure of a second percutaneous catheter drainage attempt. There were no

TABLE 4.

Organisms	Monomicrobial Isolates (8 Patients)	Polymicrobial Isolates (18 Patients)	Total
Gram-negative aerobes			
E. coli	4	8	12
Klebsiella	0	4	4
Proteus	0	2	2
Serratia	0	1	1
Morganella	0	1	1
Acinetobacter	0	1	1
Eikinella	0	1	1
Gram-positive aerobes			
Streptococcus faecalis	0	4	4
β-Streptococcus	0	2	2
α-Streptococcus	1	0	1
Gram-negative anaerobes			
Fusobacterium nucleatum	1	4	5
B. fragilis	0	7	7
Bacteriodes species	0	3	3
"Anaerobic gram-negative cocci"	0	1	1
Gram-positive anaerobes			
Peptostreptococci	0	6	6
Anaerobic diphtheroids	2	2	4
Lactobacillus	0	1	1

TABLE 5. *Origin of Pyogenic Abscess*

	At Time of Therapy	Determined During Therapy	Total
Cholecystitis/cholangitis	5	2	7
Biliary tract malignancy	2	0	2
Colon	2	3	5
Local penetrating trauma	3	0	3
Hematogenous seeding	0	3	3
Recent gastric or duodenal surgery	2	0	2
Unknown	—	4	4
Total	14	12	26

TABLE 6. *Therapy and Outcome*

Initial Therapy	No. of Patients	Outcome (No. of Patients) Cure	Treatment Failure	Death	Comments
Medical therapy					
Antibiotics alone	1	0	0	1	Diagnosis not established before death
Single aspiration and antibiotics	1	0	1	0	Percutaneous drainage successful in treatment failure
Antibiotics, cholecystectomy, or removal of T-tube	3	3	0	0	All with multiple microabscesses and ascending cholangitis
Drainage procedure					
Percutaneous drainage and antibiotics	9	5	4	0	Two patients treated with percutaneous catheter; two patients taken to surgical drainage (see text)
Surgical drainage and antibiotics	8	5	1	2	See text
Cholecystectomy, surgical drainage, and antibiotics	4	4	0	0	—

deaths in this group. Two complications were seen in the 13 patients who had diagnostic aspiration; abscess spillage necessitating immediate surgery occurred in one patient and hemorrhage necessitating transfusion in another. No complications arising from therapeutic drainage were seen.

Twelve patients had surgical drainage as initial therapy. Four patients with cholecystitis recognized on admission were successfully treated with cholecystectomy and operative drainage of the abscess. The other eight patients had operative drainage for a variety of reasons. In two of these patients, a single aspiration followed by treatment with antibiotics had failed at another hospital. One patient had an acute abdomen, one had spillage during diagnostic aspiration, and for four, two of whom were gravely ill, it was the clinician's choice. There was one treatment failure and two deaths in the patients that had surgical drainage. One patient had successfully repetitive surgical drainage 10 days after the first drainage, when the abscess failed to resolve. Another patient, in whom diagnosis was delayed, died after surgical drainage. The other patient died during operation for multiple abscesses. Two of the three patients with microabscesses were successfully treated with cholecystectomy, T-tube drainage, and antibiotics. The other patient was treated by antibiotics and removal of a T-tube previously placed.

The overall deaths were three of 26 (mortality rate: 11.5%). Analysis of the three deaths showed three common features: significant delay in diagnosis and treatment, high APACHE II scores, and origin of the abscess from the biliary tree. The patient that was diagnosed after death had an acute abdomen and sepsis. Exploratory laparotomy did not reveal any abnormalities. Blood cultures were positive for *Escherichia coli,* and the patient died from sepsis on the 10th hospital day. Necropsy showed a pyogenic abscess deep in the liver parenchyma associated with cholangitis. Culture of the biliary tree and abscess grew a pure culture of *E. coli.* In the other two deaths, there was a significant delay in diagnosis (7 and 8 days). One patient died during operation for multiple abscesses that surrounded the inferior vena cava, and the other patient died from multiorgan failure 14 days after surgical drainage. The mean APACHE II scores of the patients that died was 26.3 compared with 7.1 for the group of patients that were cured. Of the 23 surviving patients, follow-up information was available in 17 patients at 6 months without evidence of recurrence.

Discussion

In this review, we have been able to assess the impact of both imaging modalities (CT scanning and ultraso-

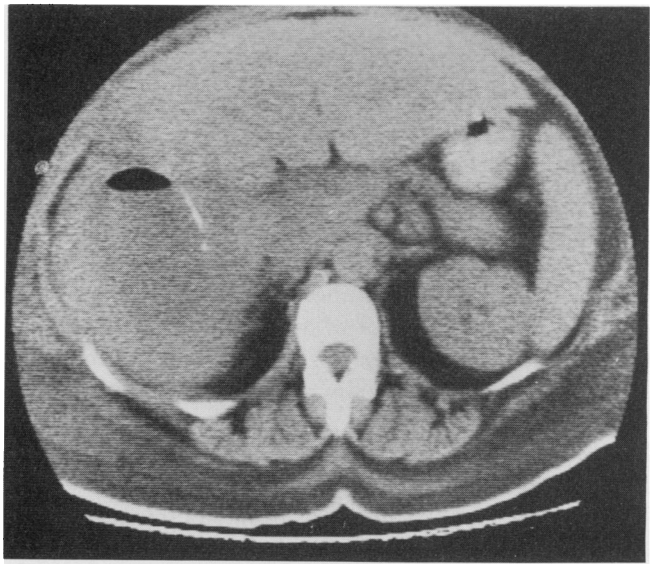

FIG. 1. Pyogenic abscess for which two efforts at percutaneous drainage failed.

nography) in expediting the diagnosis and the effect of percutaneous drainage on the clinical course and outcome of patients with pyogenic liver abscess. Most previously reported series include patients from several decades before the advent of these new techniques.[1–3,9,10]

The clinical presentation of pyogenic liver abscess remains insidious and may be protracted. Often the signs on physical examination and symptoms of a liver abscess are nonspecific; in our experience, the cholestatic pattern of liver function enzyme abnormalities is suggestive but not specific of a hepatic abscess. Fever, right upper quadrant tenderness, elevated venous leukocyte count, and hypoalbuminemia are present in most patients. The use of the APACHE II scoring system proved useful in identifying patients with a poor outcome.

The microbiologic findings for this group of patients showed the usual predominance of anaerobes and gram-negative aerobic bacilli. Since the advent of anaerobic cultures, non–spore-forming anaerobic bacteria have been recognized as important pathogens in pyogenic liver abscess and are recovered in 25–45% of cases.[11] We observed polymicrobial isolates in 69% of patients. Earlier studies have reported an increase in mortality rate with polymicrobial isolates,[3] although we did not observe this event in this small series. Bacteriologic results are generally not helpful in identifying the source of the pyogenic liver abscess, although multiple anaerobic isolates point to the colon as a source and a single isolate of *E. coli* often indicates the biliary tree as a nidus.

The optimal choice of antibiotics in liver abscess is unknown, although experimental evidence supports the use of agents active against both gram-negative aerobes and anaerobes. Most anaerobes originating in the abdomen are susceptible to similar antibiotics, and sensitivity testing is unreliable in routine anaerobiologic laboratories. The traditional use of an aminoglycoside combined with clindamycin or metronidazole is still recommended.[13] Both metronidazole and clindamycin have wide anaerobic coverage, excellent penetration to abscess cavities, and minimal side effects with short-term use. Third-generation cephalosporins have excellent activity but lack coverage for some gram-negative aerobes and anaerobes, especially *Bacteroides fragilis* (which was present in seven of our patients). The final choice of antibiotics should be guided by a culture. The duration of antibiotic therapy is controversial, but we agree with many reports that recommended therapy for 6 weeks.[14,15] When there is adequate drainage, we also feel that antibiotics should be given for 7 days after resolution of the abscess cavity and clinical signs of toxicity.

With the use of modern imaging procedures, the ability to diagnose pyogenic liver abscess is markedly improved from the past. In early studies, as many as 30% of patients with hepatic abscesses were diagnosed after death, whereas in this study 25 of 26 patients were diagnosed before death. The median time from admission to diagnosis was 2 days, which is a significant improvement from even recent studies that report the time to diagnosis range from 6.5 to 23 days.[3,16] We attributed this improvement to the sensitivity and accuracy of ultrasonography and CT scanning and aspiration of the abscess. Diagnosis is now possible with a high degree of certainty without surgical confirmation. Ultrasonography has a reported sensitivity of detecting pyogenic liver abscesses in the range of 85–95% and CT scanning of 95–100%.[17,18] Ultrasonography has the advantage of accurately visualizing the biliary tree and is better than CT scanning in distinguishing solid from cystic structures, but ultrasonography is limited by technical factors. Certain areas of the liver are difficult to visualize by ultrasonographic examination. These include areas adjacent to the hemidiaphragm, where visualization is difficult when the liver is anatomically situated high under the rib cage. Extremely obese patients and those who are uncooperative are difficult to scan with ultrasonography. Two false-negative results by ultrasonography in this study were in patients with nonhomogenous livers. In this regard, the CT scan is more sensitive and can distinguish subtle differences in density. CT scanning also has the advantage of visualizing the posterior, superior aspect of the liver. The CT scan best demonstrates surrounding structures, but both ultrasonography and CT scanning may be used to look for sources of sepsis outside the liver (i.e., kidney). Because of the common association of pyogenic liver abscesses with biliary disease, both ultrasonographic examination and CT scans may be useful to identify cholelithiasis or biliary obstruction. The technetium scan[17] adds little to the information available from ultrasonographic examination and CT scan and should never be used alone in assessing suspected liver abscesses.

Neither ultrasonography or CT scanning are accurate in differentiating loculations from multiple separate liver abscesses. Because it is requisite to drain all liver abscesses when there is more than one, any significant loculation may necessitate placement of a second catheter to improve drainage. Gerzoff et al.[19] and Bernardino et al.[20] reported that most loculations seen by ultrasonographic examination or CT scans are pseudoloculations and communicate freely within the abscess cavity. When significant loculations occur, they can potentially be a source of an inadequate percutaneous drainage and treatment failure but are not contraindications to percutaneous drainage.[21]

Determination of the origin of pyogenic liver abscess is important because it impacts on therapy. In this study the origin was determined in 14 of 26 patients at the time of therapy and later in the other eight patients. Barium enema was useful in this small series in detecting occult colonic disease, especially peridiverticular abscess. The source of the abscess was not apparent even after extensive investigation in four patients. So-called cryptogenic liver abscesses account for approximately 20% of cases, even in recent studies.[10] Biliary tract disease accounted for nine cases and is the most common underlying origin being reported.[1,22] Malignant biliary tract obstruction is becoming an increasingly significant source for pyogenic liver abscess.[3]

The source and characteristics of the abscess and the patient's underlying clinical condition are important parameters in determining therapy.

It appears that multiple microabscesses will predictably respond to systemic antibiotics.[23] However, it is important to determine the source of such abscesses because multiple small abscesses usually occur with co-existing cholangitis. In this series all three patients with multiple microscopic abscesses had ascending cholangitis necessitating additional corrective surgery on the biliary tree.

For single or multiple macroscopic abscesses, it is becoming increasingly clear that continuous drainage is necessary, either surgically or percutaneously. Since the report of McFazėdean et al.[24] report in 1953, there has been controversy over the role of medical management alone in the treatment of pyogenic liver abscess. Subsequently, there has been a number of case reports[14,25–28] of the successful therapeutic management of pyogenic liver abscess without a drainage procedure (antibiotics alone or a single aspiration followed by antibiotics). In this series the one patient who did not have a drainage procedure because of failed diagnosis died later, despite continuous antibiotic therapy. In another patient, single aspiration followed by antibiotics was unsuccessful. In two referred patients single aspiration followed by antibiotic treatment had failed. McKorkell and Niles[29] reported on a series of 14 patients that medical management was successful in only one patient and concluded that medical management is not likely to be successful. In other studies[4,9,10,16] mortality rates for patients not receiving drainage procedures ranged from 70 to 100%. Although medical management may be successful in a small percentage of patients, we believe that continuous drainage is required for optimal therapy.

The experience with the use of closed continuous percutaneous drainage of pyogenic liver abscess continues to expand.[5,18,19,20,30–33] Initial studies reported a high success rate with few complications. Nine of our patients had percutaneous drainage as the initial procedure, and it was unsuccessful in four (44%). In three of these patients the failure of the abscess to resolve necessitated the placement of a second percutaneous catheter. The failure rate and complications of percutaneous drainage of pyogenic liver abscess have been reviewed in the English literature,[19] with a reported failure rate of approximately 15% and a complication rate of 4%. Because of the high success rate, particularly in gravely ill patients, closed continuous percutaneous drainage should be the initial drainage procedure, provided there is no other indication for laparotomy and percutaneous drainage is technically feasible.[34] For those patients in whom the source of the abscess is not obvious, percutaneous drainage can be used as a temporizing measure. The optimal time of catheter removal is not known. We have adopted a policy of obtaining serial imaging studies and removing the catheter when the abscess cavity has collapsed around the catheter and drainage has ceased. Many studies reported the time to catheter removal to be between 16 and 20 days, although Johnson et al.[33] reported successful treatment of pyogenic liver abscess with only 3–4 days of catheter drainage.

Laparotomy with surgical drainage has an important role in the management of pyogenic liver abscess. Although studies from the era before CT scans and ultrasonic imaging reported a significant mortality rate with operative drainage, these historic observations are no longer valid because of improved preoperative, operative, and postoperative care as well as more timely diagnosis. Operative drainage is highly effective and now has a low mortality and morbidity rates in the management of patients with pyogenic liver abscess. There are no controlled studies comparing percutaneous with operative drainage of liver abscesses. In patients with an identified intra-abdominal source of the liver abscess as an indication for laparotomy, surgical drainage is the procedure of choice. For abscesses in which percutaneous drainage has failed or abscesses in which percutaneous drainage is not technically feasible, surgical drainage is the preferred treatment. Furthermore, surgery is often essential in eliminating the source of infections that seeded the liver, as was necessary in eight of the 12 patients coming to operation.

Overall, three of 26 patients in this study died (mortality rate: 11.5%). In an analysis of the three deaths, we found delay in diagnosis, a biliary source, and a high APACHE II score were significant factors. Other authors have reported a mortality rate of 10–20%, which has significantly improved even from reports of 10 years ago. We feel this improved mortality rate reflects the improved capability for early diagnosis and rapid application of therapy. Successful management of pyogenic liver abscess entails an individualized approach based on the underlying clinical condition and source of the abscess and rapid institution of therapy. The reduced mortality rate of pyogenic liver abscess reflects the improved capability of rapid diagnosis and individualized therapy based on underlying severity of illness and knowledge of the source of the abscess.

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