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BRIEF ARTICLE

# Pyogenic liver abscess: An audit of 10 years' experience

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## Abstract

**AIM:** To describe our own experience with pyogenic liver abscesses over the past 10 years and investigate the risk factors associated with failure of initial percutaneous therapy.

**METHODS:** A retrospective study of records of 63 PLA patients presenting between 1998 and 2008 to Australian tertiary referral centre, were reviewed. Amoebic and hydatid abscesses were excluded. Demographic, clinical, radiological, and microbiological characteristics, as well as surgical/radiological interventions, were recorded.

**RESULTS:** Sixty-three patients (42 males, 21 females) aged 65 (± 14) years [mean ± (SD)] had prodromal symptoms for a median (interquartile range; IQR) of 7 (5-14) d. Only 59% of patients were febrile at presentation; however, the serum C-reactive protein was elevated in all 47 in whom it was measured. Liver function tests were non-specifically abnormal. 67% of patients had a solitary abscess, while 32% had > 3 abscesses with a median (IQR) diameter of 6.3 (4-9) cm. Causative organisms were: *Streptococcus milleri* 25%, *Klebsiella pneumoniae* 21%, and *Escherichia coli* 16%. A presumptive cryptogenic cause was most common (34%). Four patients died in this series: one from sepsis, two from advanced cancer, and one from acute myocardial infarction. The initial procedure was radiological aspiration ± drainage in 54 and surgery in two patients. 17% underwent surgical management during their hospitalization. Serum hypoalbuminaemia [mean (95% CI): 32 (29-35) g/L *vs* 28 (25-31) g/L, $P = 0.045$] on presentation was found to be the only factor related to failure of initial percutaneous therapy on univariate analysis.

**CONCLUSION:** PLA is a diagnostic challenge, because the presentation of this condition is non-specific. Intravenous antibiotics and radiological drainage in the first instance allows resolution of most PLAs; However, a small proportion of patients still require surgical drainage.



**Key words:** Pyogenic liver abscess; Image guided drainage; Surgical drainage; C-reactive protein; Hypoalbuminaemia

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## INTRODUCTION

The management of pyogenic liver abscesses is changing. Depending on the cause and local expertise, a varying proportion of patients are treated with antibiotics

alone, surgical therapy or radiological intervention, or a combination of the above. However, there appears to be an overall trend for antibiotics and radiological intervention (either drainage or aspiration) to be the initial treatment of choice[1]. Surgical management is increasingly limited to cases of failed radiological management or to the management of complications[2-5].

Furthermore, there is an increasing recognition that pyogenic liver abscesses seen in Western and Asian countries differ in demographic characteristics, aetiological factors, and clinical behaviour. Many of the recent large case series are from South East Asian institutions, where a large proportion of pyogenic liver abscesses are caused by Klebsiella pneumoniae. These abscesses are typically associated with diabetes or a cryptogenic aetiology[5-7]. This contrasts with the predominance of *Escherichia coli* pyogenic liver abscesses of biliary aetiology found in Western institutions.

Continued changes to the management and aetiology of this disease entity prompted us to review it and describe our own experience with pyogenic liver abscesses over the past 10 years. In addition, we aim to investigate the risk factors associated with failure of initial percutaneous therapy.

## MATERIALS AND METHODS

A retrospective study of all patients treated at Royal North Shore and affiliated hospitals for pyogenic liver abscesses was conducted. A list of patients was generated by accessing the ICD-10 codes of the hospital admissions database, which dated back to 1996. This data was augmented with data from individual (upper gastrointestinal) surgeons' databases to ensure that all possible treated patients during the study period were captured. A total of 63 patients were identified during the study period of August 1998 to November 2008. The diagnosis of pyogenic liver abscess was based upon clinical features, evidence from imaging studies (ultrasound or computed tomography), as well as microbiology (blood or aspirate culture results). Liver abscesses with demonstrated positive amoebic or hydatid serology were excluded.

Basic demographic characteristics (history, examination and investigation findings at presentation), radiological/microbiological results, antibiotic use, and surgical/radiological intervention were reviewed and recorded on a standardised data sheet.

For the purposes of data recording, the examination findings of the patients were defined by the findings from the first examination by senior surgical or medical staff (registrar or above). The degree of peritonism and the location of tenderness were recorded. The presence of fever was defined as a temperature taken within the first 24 h of presentation of greater than 37.5℃. All other vital signs were defined by the first available set of observations after presentation. Tachycardia was defined as a heart rate greater than or equal to 100 beats per minute, and hypotension as a systolic blood pressure of less than 100 mmHg. For blood test results, the first available test within the first 48 h of presentation was used for analysis. Reference ranges of laboratory tests were defined by the reference ranges supplied by the local laboratory, Pacific Laboratory Medicine Services-these are included in results of Table 1. Acute renal failure was defined as an increase in the serum creatinine level of 50% over the baseline. With regards to imaging findings, the size of the abscess was defined by its greatest diameter, and in cases with multiple abscesses, as the greatest dimension of the largest abscess. Radiological intervention was subdivided into drainage and aspiration, depending on whether a drain was left in situ. The presumptive aetiology of the liver abscess was a subjective judgement made by either the treating team at the time or retrospectively by the investigators. A standard protocol for investigation of the underlying cause of the liver abscess was not used.

At our unit, patients with suspected or proven pyogenic liver abscesses are managed initially by empirical broad spectrum intravenous antibiotics, usually a combination of a third generation cephalosporin, such as ceftriaxone, along with metronidazole. The penicillin-based combination with ampicillin, an aminoglycoside (such as gentamicin), and metronidazole is also commonly used. The antibiotic regimen is modified according to response to initial therapy and available microbiology results, in consultation with the local microbiology team. Antibiotics are generally continued for 4-6 wk, with the initial 2 wk is administered intravenously. First line intervention is radiological drainage of the liver abscess. This is performed with sedation and local anaesthesia under computed tomography or ultrasound control. Typically, a "pigtail" drain (8-12 French) is placed into the abscess, which is then left on free drainage with or without periodic normal saline flushes. Repeated procedures may be indicated. In some cases, rather than placing an indwelling drain, radiological guided aspiration was used as the first line treatment. The choice of indwelling drain or aspiration depends on clinician preference, but aspiration is generally only used when the abscess is small or multiple. Indications for surgical intervention or drainage include - signs of peritonitis, ruptured abscesses, abscesses not responding to antibiotics and drainage, and multiloculation.

All statistical analysis and plotting were performed with Intercooled Stata version 9.1 (Statacorp, Texas, USA). Note that, because of missing data for certain characteristics, some denominators of proportion statistics are not consistently equal to 63 (the full cohort of subjects).

## RESULTS

### *Demographic characteristics and presentation*

Sixty-three patients (42 males and 21 females) were identified for this study, with a mean (SD, range) age of 64 (14, 31-97) years. The peak incidence was in the 8th decade of life (70-79 years). Almost a quarter of patients (15/62, 24%) had a history of gallstones or cholecystectomy. Nearly a quarter of patients ($n$ = 14) had a history (past or current) of malignancy at presentation. Of these, 10 (16%)

**Table 1 Summary of laboratory results at initial presentation**

| | Reference range | No. of patients measured | mean ± SD | % of patients outside reference range |
|---|---|---|---|---|
| White cell count (× $10^9$/L) | 4.0-11.0 | 62 | 15.0 ± 6.3 | 74% |
| Neutrophil count (× $10^9$/L) | 2.0-8.0 | 62 | 12.9 ± 5..9 | 82% |
| Haemoglobin (g/L) | 135-180 | 62 | 118 ± 21 | 24% Hb < 100 g/L |
| Platelets (× $10^9$/L) | 150-400 | | 320 ± 202 | 42% |
| C-reactive protein (mg/L) | < 5 | 47 | 272 ± 119 | 100% (47/47) |
| Urea (mmol/L) | 3.1-8.1 | 62 | 8.2 ± 5.96 | 29% Urea > 8.1 mmol/L |
| Creatinine (μmol/L) | 60-100 | 62 | 105 ± 60 | 42% Cr > 100 μmol/L<br>16% Cr > 150 μmol/L |
| Albumin (g/L) | 35-46 | 62 | 30 ± 7.0 | 73% |
| AST (U/L) | 12-36 | 61 | 127 ± 301 | 67% |
| ALT (U/L) | 5-40 | 62 | 118 ± 222 | 73% |
| ALP (U/L) | 41-119 | 61 | 209 ± 140 | 71% |
| GGT (U/L) | 5-65 | 62 | 191 ± 201 | 75% |
| Bilirubin (μmol/L) | 3-18 | 61 | 30 ± 39 | 54% Bil > 18 μmol/L<br>13% Bil > 50 μmol/L |
| Glucose (mmol/L) | 3.5-5.5 | 47 | 7.8 ± 2.6 | 15% (7/47) Glucose > 10 mmol/L |
| INR | ≤1.5 | 53 | 1.3 ± 0.56 | 13% (7/53) |

AST: Aspartate transaminase; ALT: Alanine transaminase; ALP: Alkaline phosphatase; Bil: Serum bilirubin; GGT: γ glutamyl transpeptidase; INR: International normalized ratio; RR: Reference range. Reference ranges supplied by local pathology laboratory.

**Table 2 Summary of physical examination findings on presentation**

| Clinical finding | *n* (%) |
|---|---|
| Fever (T > 37.5) | 33 (59) |
| Hypotension (SBP < 100) | 7 (13) |
| Tachycardia (HR ≥ 100) | 29 (52) |
| Peritonism | |
| None | 49 (86) |
| Localized guarding | 8 (14) |
| Generalized peritonism | 0 (0) |
| Location of tenderness | |
| Non tender abdomen | 20 (35) |
| Right upper quadrant | 22 (39) |
| Other abdominal tenderness | 15 (26) |

HR: Heart rate in beats per minute; SBP: Systolic blood pressure in mmHg; T: Body temperature in degrees Celsiu.

had a current diagnosis of malignancy: three with cholangiocarcinoma, three with pancreatic cancer, and one each with colon cancer, gastric cancer, prostate cancer, and follicular dendritic cell tumour of the liver. Only 13% (8/62) had a history of diabetes mellitus.

The median (IQR) duration of symptoms prior to presentation was 7 (5-14) d. Table 2 summarises the presentation of these patients. Note that the presence of fever and tachycardia was found in only slightly more than half of the patients. It was uncommon for patients to be hypotensive on presentation. Abdominal signs were non-specific in most cases.

The initial laboratory results were available for all but one patient. They are summarised in Table 2. Markers of inflammation [white cell count, neutrophil count, and the serum C-reactive protein (CRP)] were generally raised. In particular, CRP was elevated in all of the 47 tested patients.

Forty-two percent of patients had elevated serum creatinine levels, but only 16% had a serum creatinine of greater than 150 μmol/L at presentation. Liver enzymes were each elevated in about 70% of the patients. Serum bilirubin was elevated in slightly more than half of the patients, but only 13% had a clinically significant hyperbilirubinaemia of greater than 50 μmol/L. Only 15% of the subjects had a blood glucose level of greater than 10 mmol/L.

### Imaging

Computer tomography was used in all patients, but the initial diagnosis was made with abdominal ultrasonography in 14 cases. Detailed imaging reports or films were available for 60 patients. Sixty-seven percent had solitary liver abscesses: one patient had two abscesses and 32% had three or more abscesses. The median (IQR) maximum dimension of liver abscesses was 6.3 (4.0-9.0) cm. Note that in five cases multiple "microabscesses" (< 1 cm diameter) were identified. Sixty-six percent had involvement of the right liver only, 19% had left liver involvement only, and 15% (9/58) had bilateral involvement. Twelve percent demonstrated evidence of gas formation within the abscess and 15% had imaging evidence of biliary dilatation.

### Microbiology and aetiology

Although all 63 patients had either culture of blood or of the abscess, the causative organism was identified in only 50 (79%). The yield from liver abscess aspirate, 67%, was higher than from blood cultures (48%). The most common causative pathogens were *Streptococcus milleri* 25%, Klebsiella pneumoniae 21%, and *Escherichia coli* 16% (Table 3). Note that many patients had more than one set of cultures taken during the study period. In one patient the abscess culture grew Corynebacterium urealyticum but blood cultures grew Staphylococcus aureus; however, that was likely to be a skin contaminant.

The aetiology of the abscess was only evident in 59 patients (Table 4). *Streptococcus milleri* was associated with

**Table 3 Summary of microbiology results for blood culture results, liver abscess aspirate culture results, and presumed causative pathogen**

| Organism | *n* (% of patients with culture results) | | |
|---|---|---|---|
| | Positive blood cultures | Positive liver aspirate cultures | Causative pathogen |
| *Streptococcus milleri* | 8 (14) | 12 (24) | 16 (25) |
| *Klebsiella species* | 9 (16) | 8 (16) | 13 (21) |
| *K. pneumoniae* | 7 | 8 | 11 |
| *K. oxytoca* | 1 | 0 | 1 |
| *K. terrigena* | 1 | 0 | 1 |
| *Escherichia coli* | 6 (11) | 3 (5.9) | 10 (16) |
| Mixed[1] | 2 (3.6) | 6 (12) | 5 (8) |
| *Fusobacterium necrophorum* | 1 (1.8) | 1 (2.0) | 2 (3.2) |
| *Pseudomonas aeruginosa* | 0 (0) | 1 (2.0) | 1 (1.6) |
| *Lactobacillus* | 0 (0) | 1 (2.0) | 1 (1.6) |
| *Corynebacterium urealyticum* | 0 (0) | 1 (2.0) | 1 (1.6) |
| *Citrobacter koseri* | 0 (0) | 1 (2.0) | 1 (1.6) |
| *Staphylococcus aureus*[2] | 1 (1.8) | 0 (0) | 0 (0) |
| Causative organism not identified | - | - | 13 (21) |
| Total negative | 29 (52) | 17 (33) | - |
| Total positive | 27 (48) | 34 (67) | 50 (79) |
| Total number of patients with available culture results | /55 | /51 | /63 |

[1]Includes 2 cases of *Clostridium perfringens*; [2]Discordant with liver abscess microbiology. Likely contaminant.

**Table 4 Summary of the presumed aetiology of the patients' pyogenic liver abscesses**

| Aetiology | *n* (%) |
|---|---|
| Cryptogenic | 20 (34) |
| Biliary | 14 (22) |
| Portal (e.g. appendicitis, diverticulitis) | 12 (20) |
| Haematogenous (other bacteremic source) | 7 (11) |
| Direct (e.g. pericholecystic abscess, RFA) | 6 (9.4) |

RFA: Radiofrequency ablation.

**Table 5 Summary of interventions**

| Initial intervention (%) | | → | Secondary intervention (%) | | → | Further interventions (%) | |
|---|---|---|---|---|---|---|---|
| AB | 5 (7.9) | → | RA | 1/5 (20) | | | |
| | | | Other | 1/5 (20) | | | |
| RD | 43 (68) | → | RA | 1/43 (2.3) | | | |
| | | | SG | 5/43 (12) | | | |
| | | | RD | 13/43 (30) | → | SG | 1/13 (7.7) |
| | | | | | | RD | 3/13 (23) |
| RA | 11 (18) | → | RD | 2/11 (18) | | | |
| | | | SG | 2/11 (18) | | | |
| SG | 2 (3.2) | | - | | | - | |
| Other | 2 (3.2) | → | SG | 1/2 (50) | | | |

AB: Antibiotics only; RA: Image guided aspiration of abscess; RD: Image guided insertion of indwelling drain; SG: Surgical intervention. Note that all patients received intravenous antibiotics before any interventional treatment.

portal sepsis in 4/12, *Escherichia coli* was associated with biliary sepsis in 5/14, and Klebsiella species was associated with cryptogenic sepsis in 7/20.

There were two cases on *Clostridium perfringens*-both were isolated as mixed growths on cultures. Organisms isolated with Clostridium perfringens in these cases were *Escherichia coli* and *Enterococcus faecalis* in one case, and *Enterococcus faecalis* and *Citrobacter freundii* in the other. One of the patients had rapidly progressing sepsis and underwent a laparoscopy; however, the patient rapidly deteriorated. The second patient developed sudden onset of severe sepsis following radiofrequency ablation (RFA) of a liver metastasis. She underwent radiological guided drainage of the liver abscess and eventually thoracotomy for decortication and drainage. She returned to good health but died of progression of her pancreatic cancer six months later.

### Intervention

Five patients were treated by intravenous antibiotics followed by oral antibiotics, without any need for other intervention (Table 5). Radiological drainage was the most frequent initial intervention, which was used in 43 (68%) cases. Of these, almost a third required a second drainage/aspiration procedure and of these, three required further drainage procedures. In this group, surgery was eventually required in six (14%) cases. Eleven patients were initially treated with image-guided aspiration of the liver abscess. Of these, two required drain placement, and a further two required surgical drainage. Surgical drainage was performed as the initial procedure in two (3.2%) of patients. In total, 11 patients (17%) underwent surgical drainage or resection.

Two patients had other types of initial intervention. One had endoscopic retrograde cholangiopancreatography (ERCP), sphincterotomy, and removal of choledocholithiasis for biliary sepsis. Another patient had a laparoscopic appendicectomy. In both cases, the pyogenic liver abscesses were small and thought to be secondary to biliary/portal pyaemia. The patient with biliary sepsis eventually required a laparoscopic cholecystectomy and

**Table 6 Complications occurring in 21 patients**

| Complication | *n* |
|---|---|
| Acute renal failure | 7 |
| Abdominal collection/sepsis | 4 |
| Thoracic empyema/large pleural effusion requiring surgical drainage | 4 |
| Multiple organ failure | 2 |
| Biliary fistula | 2 |
| Hemorrhage from percutaneous drainage | 2 |
| Portal vein thrombosis | 1 |
| Hepatic vein thrombosis | 1 |
| Subcapsular hematoma from percutaneous drainage | 1 |
| Myocardial infarction | 1 |
| Necrosis of terminal phalanges | 1 |

bile duct exploration due to failed endoscopic retrieval of choledocholithiases.

Other forms of surgical interventions were performed because of pleural sepsis requiring drainage of pleural empyema and decortications of lung ($n = 4$).

Indications for surgery as the initial management in two cases were as follows: peritonitis on clinical examination requiring laparoscopy (which was converted to laparotomy), and sepsis in a patient on cyclosporin, methotrexate, and prednisolone for rheumatoid arthritis.

Indications for surgical intervention as a subsequent procedure included: leakage of abscess from a percutaneous drainage, haemorrhage from percutaneous drainage ($n = 2$), failure of resolution or recurrence of the abscess ($n = 4$), and laparoscopic cholecystectomy for an intrahepatic extension of a pericholecystic abscess ($n = 1$).

### Complications and outcomes

Twenty-one patients (33%) developed complications (Table 6) that were directly related to the sepsis or abscess and which required specific intervention.

In two patients, the abscess ruptured through the upper surface of the liver into the pleural cavity: one was related to the placement of a drain and the other was related to a subphrenic abscess. A further patient developed a large thoracic empyema related to her subphrenic abscess and one developed a large fibrinous pleural effusion with no pus.

Two patients had severe haemorrhage associated with the radiological intervention (ultrasound guided drain placement and computed tomography (CT) guided aspiration/biopsy) and required resection of the liver segment that contained the abscess.

The systemic effects of the sepsis were severe enough to cause acute renal failure in seven patients and multiorgan failure in two. A patient who presented with severe shock was treated in Intensive Care with antibiotics and inotropes and he gradually recovered; however, he developed necrosis of the terminal phalanges of his hands and feet. He was well enough to be discharged to the ward, but because of recurrence of sepsis, surgical opinion was sought. He required drainage of the abscess and associated cholecystectomy, which was successfully treated by laparoscopic approach, following which he rapidly recovered and was discharged.

Two patients developed biliary fistulae post radiological drainage. One patient underwent biliary decompression with ERCP and nasobiliary drainage, which resolved the fistulae. The second patient had a history of a cholangiocarcinoma resected with roux-en-Y and hepaticojejunostomy eight months prior to the development of her multiple liver abscesses. Three CT guided percutaneous drains were inserted following which she developed a controlled biliary fistula through one of the drains. Following choledoschoscopy, which showed no tumour recurrence, the drain was removed but recurrent abscesses occurred. A percutaneous drain guided surgical debridement was undertaken and sepsis settled; however, a chronically low-volume draining fistula remained. She was discharged home to independent living, but after five months became unwell again and decided to accept palliative care.

Four patients died during the hospital admission. One patient who had a severe sepsis due to *Clostridium perfringens* underwent a desperate surgical procedure but, not unexpectedly, the resuscitation failed. Two died from progression of pancreatic cancer managed in a palliative fashion. A further patient, a 97 year old lady, died from a cardiac arrest secondary to acute myocardial infarction six days after the insertion of a percutaneous drain.

### Risk factors predicting failure of initial percutaneous therapy

Table 7 summarises the results of univariate analysis of factors that predict the failure of initial percutaneous therapy. A low serum albumin level was the only statistically significant factor found to be associated with failure of initial percutaneous therapy ($P = 0.045$). Importantly, the initial type of percutaneous therapy (drain *vs* aspiration) was not associated with initial success.

Multivariate analysis was not performed as the small number of treatment failures would mean that the event per variable rate would be unacceptably high.

## DISCUSSION

Consistent with other recent studies, most patients with liver abscesses are elderly, with a mean age of 64 years[2,8-10]. This is about 10 years older than subjects in previous reports[4,5,11]. Again, a preponderance of males was noted.

The presentation of pyogenic liver abscesses is often non-specific and its diagnosis requires a high degree of clinical suspicion. This is reflected in the finding that the median duration of symptoms of a week, with a further quarter of patients having symptoms between 1-2 wk, prior to presentation. Clinical abdominal findings were largely unhelpful, with localised peritonism found in only 14% and localised right upper quadrant tenderness in less than 40%. The literature indicates that these signs are found in 15%-55% of cases[2,4,9,11].

Laboratory tests were equally non-specific, apart from

**Table 7 Univariate analysis of factors that may lead to failure in initial percutaneous therapy**

| | Treatment successful | Treatment failure | *P*-value |
|---|---|---|---|
| Demographic characteristics and history | | | |
| Age (yr), mean (95% CI) | 67 (62-73) | 63 (57-69) | 0.26 |
| Sex (M:F) | 20:11 | 15:08 | 1.00 |
| Prodrome (days), median (IQR) | 7 (3-20) | 7 (5-14) | 0.88 |
| History of gallstone disease, *n* (%) | 8 (27) | 5 (22) | 0.76 |
| History of diabetes mellitus, *n* (%) | 4 (13) | 3 (13) | 1.00 |
| Chronic renal failure, *n* (%) | 1 (3.3) | 1 (4.4) | 1.00 |
| Current cancer, *n* (%) | 6 (20) | 5 (22) | 1.00 |
| Examination findings, *n* (%) | | | |
| Fever | 16 (53) | 12 (63) | 0.56 |
| Tachycardia | 13 (43) | 11 (58) | 0.39 |
| Hypotension | 4 (13) | 1 (5.3) | 0.64 |
| Laboratory findings, mean (95% CI) | | | |
| Leucocytes ($\times 10^9$/L) | 15.2 (13.1-17.4) | 13.6 (11.2-16.0) | 0.30 |
| Neutrophil ($\times 10^9$/L) | 12.8 (10.8-14.9) | 11.7 (9.5-13.8) | 0.43 |
| Haemoglobin (g/L) | 114 (106-121) | 120 (110-130) | 0.26 |
| Platelet ($\times 10^9$/L) | 341 (255-426) | 319 (250-388) | 0.70 |
| Urea (mmol/L) | 9.3 (6.8-11.9) | 6.5 (5.3-7.7) | 0.07 |
| Creatinine (μmol/L) | 110 (83-138) | 103 (86-121) | 0.70 |
| CRP (mg/L) | 287 (236-338) | 258 (193-324) | 0.47 |
| Albumin (g/L) | 32 (29-35) | 28 (25-31) | 0.045 |
| AST (U/L) | 187 (30-344) | 70 (43-97) | 0.19 |
| ALT (U/L) | 149 (37-260) | 84 (55-114) | 0.33 |
| GGT (U/L) | 193 (115-271) | 183 (96-269) | 0.85 |
| ALP (U/L) | 201 (154-249) | 203 (143-262) | 0.97 |
| Bilirubin (μmol/L) | 29 (13-45) | 26 (19-32) | 0.75 |
| Glucose (mmol/L) | 7.9 (6.7-9.0) | 7.6 (6.4-8.9) | 0.79 |
| INR | 1.2 (1.1-1.3) | 1.4 (1.0-1.8) | 0.24 |
| Microbiology | | | |
| Positive blood culture, *n* (%) | 12 (43) | 9 (47) | 0.78 |
| Positive aspirate culture, *n* (%) | 17 (61) | 17 (85) | 0.11 |
| Organism, *n* (%) | | | 0.19 |
| *Streptococcus milleri* | 8 (26) | 8 (35) | |
| *Klebsiella species* | 5 (16) | 7 (30) | |
| *Escherichia coli* | 6 (19) | 0 (0) | |
| Other | 6 (19) | 4 (17) | |
| Negative cultures | 6 (19) | 4 (17) | |
| Imaging findings | | | |
| Multiple abscesses, *n* (%) | 7 (24) | 10 (45) | 0.14 |
| Side of liver, *n* (%) | | | 0.10 |
| Left | 5 (17) | 2 (10) | |
| Right | 23 (77) | 13 (62) | |
| Bilateral involvement | 2 (7) | 6 (29) | |
| Abscess diameter, median (IQR) | 6.0 (3.8-9.5) | 6.5 (5.0-8.4) | 0.83 |
| Diameter > 5 cm | 11 (41) | 7 (35) | 1.00 |
| Presence of gas, *n* (%) | 5 (17) | 1 (5) | 0.38 |
| Biliary duct dilatation, *n* (%) | 6 (20) | 2 (10) | 0.45 |
| Intervention | | | |
| Percutaneous drain insertion (*vs* percutaneous aspiration) | 24 (77) | 19 (83) | 0.74 |
| Cause | | | |
| Presumptive cause, *n* (%) | | | 0.60 |
| Cryptogenic | 8 (29) | 9 (41) | |
| Biliary | 7 (25) | 5 (23) | |
| Portal | 6 (21) | 4 (18) | |
| Haematogenous | 5 (18) | 3 (14) | |
| Direct | 2 (7) | 1 (5) | |

AST: Aspartate transaminase; ALT: Alanine transaminase; ALP: Alkaline phosphatase; CRP: C-reactive protein; GGT: Gamma glutamyl transpeptidase; INR: International normalized ratio.

demonstrating signs of inflammation. Notably, not only did all tested patients have a raised serum C-reactive protein, but the levels were also significantly raised, with a mean of 272 mg/L. By comparison, only 82% of patients demonstrated neutrophilia. In addition, consistent with a systemic inflammatory response, the serum albumin was depressed in 73% of patients. CRP is not a commonly measured laboratory parameter documented in older studies: Rintoul *et al*[3] reported that all nine of their patients with PLA had a raised CRP level. However, a recent paper

by Foo *et al*[12] demonstrated that the CRP was elevated in all 133 tested patients. Whilst each of the "liver enzymes" was abnormal in about 70% of cases, neither a "cholestatic" or "hepatitic" pattern of LFT derangement predominated. In addition, mild hyperbilirubinaemia occurred in more than half of the patients, but clinically significant hyperbilirubinaemia was uncommon. These results are largely consistent with recent large case series (from both Asian and "Western" countries)[2,8,12,13].

It is interesting to note that four large Asian case series[2,5,8,12], with a total of more than 600 cases over the last ten years, demonstrated a large proportion of patients with Klebsiella species: accounting for 43% to 66% of cases. In each of these studies, the biliary tree was the most commonly identified aetiology. However, the most common aetiology overall was "cryptogenic" in the three studies, where Klebsiella species accounted for more than half of all cases. Indeed, it has been suggested that Klebsiella is associated with "cryptogenic" liver abscesses[9]. It is noted that Klebsiella liver abscess may represent a new syndrome in diabetic patients in Taiwan[5] or perhaps in Asia. Recent "Western" series, however, suggested that *Escherichia coli* is still the most common causative organism[10,13-15]. A new finding that has come to light in two papers published in 2010 from Western institutions with about 60 patients each, is the high prevalence (48% and 55%) of polymicrobial infections[14,16]. The latter study was characterised by a very large proportion of patients with malignancy (88%).

The microbiological results of the current study fall somewhere in between Asian and Western series. We found that *Streptococcus milleri* was the most common organism, followed by Klebsiella species, and then *Escherichia coli*. This perhaps reflects the most common presumptive aetiology of liver abscesses in this series: cryptogenic, biliary, and portal. It is interesting to compare our results with another Australian study published a decade ago, which found that *Escherichia coli*, *Streptococcus milleri*, and *Enterococcus faecalis*, in this order of frequency, were the most commonly isolated organisms. Thirty-eight percent of the cases in that study had a cryptogenic origin, and 48% had a biliary aetiology[4]. Interestingly, our series also had a large proportion of cryptogenic abscesses. Only 8% of all cases in our study had a polymicrobial culture result.

The first line treatment for all pyogenic liver abscesses is broad spectrum antibiotics. Our empirical antibiotic choice and duration of treatment are similar to those reported elsewhere in the literature[1,2]. Shorter durations of treatment have also been described[17].

There has been a trend for increasing use of radiological management of pyogenic liver abscesses, although the proportion of patients treated with radiological intervention varies greatly between centres[3,11,13]. Successful use of radiological intervention as the first line intervention is reflected in three large series: Wong *et al*[2] described 80 patients who were all treated either with antibiotics alone or antibiotics and percutaneous aspiration/drainage with no patients requiring surgical drainage. Two other series from Taiwan described 111/128 (87%) and 79/86 (92%) patients, respectively, who underwent radiological drainage/aspiration[5,9]. This continued trend away from surgical therapy is confirmed by three studies published this year (2010), with only 11/377 (2.9%), 1/61 (1.6%), and 5/51 (9%) requiring surgical therapy[12,14,16].

However, Tan *et al*[8] suggested that radiological aspiration may not be appropriate in all patients, and that the use of surgical drainage is advantageous in patients with abscesses larger than 5 cm, due to likely multiloculation. They found no difference in mortality or morbidity between the surgical and percutaneous drainage groups. This finding was confirmed by Alvarez Pérez *et al*[13] who described 133 consecutive patients in which they found no difference in mortality or morbidity between treatment groups (open *vs* percutaneous). Interestingly, the latter study also found that abscess size did not predict morbidity or mortality, which would appear to contradict the conclusion of Tan *et al*[8]. Consistent with this, we have found that abscess diameter did not predict failure of percutaneous therapy.

Image guided catheter drainage was favoured over radiological needle aspiration at our institution. There is no consistently favoured option in the literature, with some groups preferring needle aspiration over catheter drainage, and some *vice versa*. An early randomised study suggested that catheter drainage in patients with liver abscesses (pyogenic and amoebic) had a higher success rate compared with needle drainage alone[18]. However, a more recent randomised study did not find any statistically significant difference between the two groups[19]. Therefore, it is likely that both radiological interventions appear to be equally effective.

The need for a secondary intervention is similar between the drainage (19/43, 44%) and the aspiration groups (4/11, 36%) in this study. Indeed, no statistically significant difference in failure rate was found between the two groups. It may be noted that this "failure" rate is high compared to what is described in the literature. This may relate to the fact that approximately 90% of patients received radiological drainage as the initial procedure. It may also be related to the definition of a secondary procedure-we included repositioning and increasing the size of drains, as well as re-aspiration, as secondary procedures, whereas, in other case series, this may be considered an extension of the primary procedure. The overall rate of surgical drainage of 17% (11/63) in our series is consistent with the abovementioned studies.

Over the past few decades, the mortality associated with liver abscesses has decreased gradually. Prior to 1980, the mortality in published case series was consistently greater than 50%[1]. Improvements in mortality in the 1980s were attributed to the use of effective antibiotics. Case series with study periods in the 1980s demonstrated a mortality rate of between 13%-18%[11,20]. Further improvements in mortality then occurred due to the advent of cross sectional imaging with computed tomography and ultrasonography. The mortality rate for studies with study periods during and after 1990s was between 4%-10%[2,4,5,8,9,19]. The mortality rate in the current study was 6.3%, continuing this trend for improving mortality.

This can be compared with the mortality of 8% in another Australian case series by Barakate *et al*[4], which had a study period of a decade earlier than our current study. The deaths that occurred in both these studies principally occurred in already infirm patients, such as those with advanced cancer. The association of mortality with malignancy is reflected in the high mortality rate of 29% in a recent study by Mezhir *et al*[16] where 88% of patients had a history of malignancy.

Many studies have investigated the risk factors for morbidity and mortality of the disease. However, as the mortality (and to a lesser extent, morbidity) has decreased, the focus has shifted to identifying patients who would successfully be treated with percutaneous therapy. Mezhir *et al*[16] have found that the presence of yeast and communication with an untreated biliary obstruction were associated with failure of percutaneous therapy. Our current study has focused on the failure of initial percutaneous therapy and has found hypoalbuminaemia to be associated with failure. Hypoalbuminaemia may be associated with failure of initial therapy owing to its association with the severity of the underlying septic process.

Unlike mortality, morbidity is more difficult to compare between studies, because of differences in completeness of data collection in retrospective studies and therefore tends to be under-reported. Complications such as biliary fistula, leakage, and haemorrhage following percutaneous drainage or aspiration are known, but uncommon, complications. Tan *et al*[8] described in the percutaneous drainage group ($n$ = 36), one patient (2.8%) with fistula formation and four patients (11%) with peritonitis post drainage. This is similar to our reported rates of bile fistula and abdominal sepsis. Hemoperitoneum after needle aspiration has also been described-Yu *et al*[19] had one such patient in a series with 64 patients. Furthermore, there are large case series, such as Wong *et al*[2] with 80 patients who underwent percutaneous aspiration, that report no "major" complications. Operative management of liver abscesses may be associated with significant morbidity. In a study of 32 patients who underwent operative management (either for failed drainage or presenting as a surgical emergency), Christein *et al*[21] reported a morbidity rate of 41%. This included two patients with persistent bile leaks. A similarly high morbidity rate of 27% was described by Tan *et al*[8] in their surgical drainage group.

This is a retrospective review and was not undertaken with a standardized protocol variance in management, which could distort the conclusions; however, the surgeons involved in this study kept prospective records of their experience. The results, however, do reflect a changing trend towards a more conservative treatment protocol with an improving outcome. It provides the basis for a standardized protocol to be prospectively applied to our institution.

In conclusion, pyogenic liver abscess can be a diagnostically and therapeutically challenging problem. Often, the presentation and investigations are non-specific, although the serum CRP appears to be the simplest and most sensitive test. However, it is not specific. CT or magnetic resonance scans allows imaging of the abscess for diagnosis and assessment of progress, and also allows percutaneous image guided drainage. A combination of broad spectrum intravenous antibiotics and radiological drainage usually allows resolution of pyogenic liver abscesses. A proportion of patients will require repeat procedures-this appears to be predicted by low serum albumin at presentation. A further smaller proportion of patients will ultimately require surgical drainage.

## COMMENTS

### Background

Pyogenic liver abscesses are most frequently caused by *Escherichia coli*, *Streptococcus milleri,* or Klebsiella species often through, biliary, portal sepsis, or cryptogenic sepsis, respectively. It is a diagnostic and therapeutic challenge because patients usually present with a non-specific septic illness. Although the mortality rate has greatly improved, the occurrence of a liver abscess threatens a patient's survival if not adequately treated.

### Research frontiers

Improving the frequency of early diagnosis will depend on education of clinicians about the need for clinical suspicion aided by the finding of an elevated C-reactive protein and confirmed by radiological imaging. Early cases may be treated by antibiotics, but larger abscesses also frequently require image guided percutaneous aspiration or drainage. Surgery is only required in complex cases. Cryptogenic infections with *Klebsiella* are the most common cause in Asian series, while biliary sepsis and a portal source of sepsis are most common in Western society. This series was a mixture of the two patient groups.

### Innovations and breakthroughs

This article describes a moderate sized case series from an Australian tertiary referral centre, where patient presentation and outcome appear to be similar to other Western case series. There was a large proportion of Klebsiella organisms, indicating that the aetiology appears lie between the Asian and Western case series. This study also confirms the value of percutaneous therapy.

### Applications

This article confirms that elevated C-reactive protein level is an important guide to the diagnosis, which is frequently delayed. Intravenous antibiotics in combination with percutaneous image guided aspiration or drainage is usually a successful treatment.

### Peer review

This is a retrospective case series of 63 Australian patients with pyogenic liver abscesses. The text is generally well written, with a structured abstract and organized sections. The manuscript has scientific value since it includes relevant information about an important condition with multiple therapeutic options. I believe it can be considered for publication, provided that the authors adequately address some key issues and suggestions.

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