

Liver abscess in adults: ten years experience in a UK centre

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Summary

Background: The epidemiology and management of liver abscess (LA) have evolved over time.

Aim: To examine our experience over 10 years in a UK teaching centre.

Design: Retrospective review of patient records.

Methods: We reviewed the records of all patients aged > 16 years discharged from Royal Hallamshire Hospital with a diagnosis of LA between April 1988 and December 1999.

Results: There were 69 patients with LA (65 pyogenic, 4 amoebic), giving a crude annual incidence rate of 2.3/100 000/year (18.15/100 000 hospital admissions). Median age was 64 years. Single lesions were found in 41 patients, multiple lesions in 28. Pre-admission, patients were symptomatic for a median 14 days, with the most common symptoms and signs being fever and abdominal

pain/tenderness. Pathogens were identified in 74% and predisposing aetiology in 92% of those undergoing investigation. Spread of infection to the liver via the portal venous system was the commonest route of infection (46%), most frequently in patients aged ≥ 60 years ($p=0.019$). Abdominal ultrasound (US) was diagnostic for LA in >90% of cases. Treatment with anti-microbial therapy plus interventional radiology was optimal. The case fatality rate was 12.3%, mainly from associated underlying pathology.

Discussion: LA is commonly associated with underlying gastrointestinal pathology. Seeking out this underlying aetiology is an integral part of management. We recommend US as the first-line diagnostic tool with guided intervention plus antibiotic(s) as first-line treatment. Prognosis depends chiefly on the underlying pathology.

Introduction

In the early part of the twentieth century, liver abscess (LA) was described as a condition affecting predominantly young males in the setting of intra-abdominal infection.¹ However, in the antibiotic era, improvements in radiological diagnosis have led to the recognition of hepatobiliary pathology as the principal association.^{2–7} More recent reports have suggested an increasing incidence of LA, particularly among older people.^{8–12} Treatment of LA has changed over the last two decades of the twentieth century towards a non-surgical approach,

largely because of improved interventional radiology technique and its wider availability.^{13–15} A vigorous attempt to identify any underlying pathology is an important component of management, and a variety of approaches have been advocated. In many cases, no underlying diagnosis is established.^{8,16,17}

This study was designed to analyse the current epidemiology, diagnosis, management, predisposing factors and outcome of patients older than 16 admitted with LA from the community to a British teaching hospital.

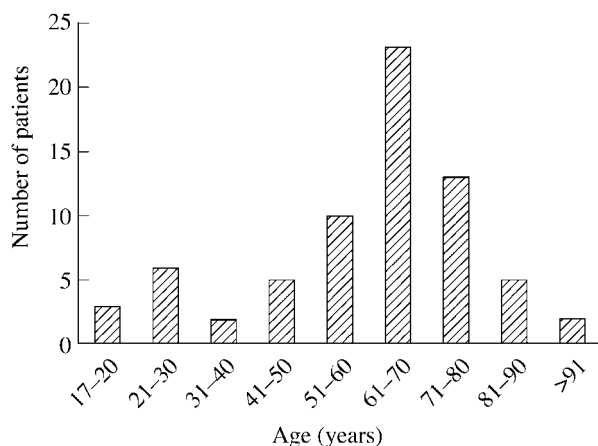


Figure 1. Age distribution of 69 patients with liver abscess.

Methods

The records of patients aged >16 years discharged from Royal Hallamshire Hospital with a diagnosis of LA between April 1988 and December 1999 were reviewed. Cases were identified through searching the hospital database of all patients discharged with the diagnosis of LA during the study period. This is likely to have underestimated the actual number of cases, as coding may have not always included patients with an associated underlying disease. Case definition required patients to have one or more filling defects on liver ultrasound examination (US) or computerized tomography (CT) together with identification of pus or complete resolution of radiological abnormalities following antimicrobial therapy. Symptoms, signs, therapeutic intervention and laboratory data on admission and during the clinical course were recorded. Predisposing factors and complications were also recorded.

LA was considered secondary to biliary tract disease in patients with gallstones and/or acute cholecystitis, or who had other documented biliary tract abnormality. It was considered secondary to

portal spread when there was documented infection or abdominal pathology in the distribution of portal vein. LA was considered cryptogenic where no obvious extra-hepatic source of infection was identified. Recurrence was defined as the development of new clinical and radiological changes subsequent to clinical and/or radiographic resolution.

During the study period, all microbiological samples were processed in a similar fashion. Cultures of specimens obtained were processed for microscopy, standard aerobic and anaerobic cultures.

Confidence interval (CI) analysis for 95%CI of proportions and Mann-Whitney analyses were performed using SPSS for Windows, v8.

Results

Of 380 000 hospital admissions in the study period, there were 69 patients with LA: 65 pyogenic (PLA) and four amoebic (ALA). Six cases were excluded because the diagnosis could not be confirmed with certainty or files were not obtainable. The crude annual incidence rate of LA in this series was 18.15 per 100 000 hospital admissions. The hospital serves an estimated population of 300 000, giving a yearly crude incidence of 2.3 cases per 100 000 population. The median age was 64 years (range 17–91, Figure 1). The male to female ratio was 1.3:1. No patient had a history of solid organ transplantation, was known to have cirrhosis, or suffered from decompensated liver disease.

Pre-hospital admission, patients were symptomatic for a median of 14 days (range 1–90). Median hospital stay was 22 days (range 5–79 days). Symptoms and signs at presentation are shown in Table 1. Results of routine haematology and biochemistry tests are shown in Table 2. Of note, 23 (33%) patients had normal liver function on admission and 10% had a normal white cell count.

Table 1 Main complaints and clinical findings on admission in 69 patients with liver abscess

Symptoms	n (%)	Signs	n (%)
Fevers	46 (67%)	Fever > 37.5 °C	48 (70%)
Abdominal pain	46 (67%)	Right hypochondrial/ abdominal tenderness	37 (54%)
Nausea and vomiting	28 (41%)	Hepatomegaly	21 (30%)
Night sweats	27 (39%)	Unremarkable	12 (17%)
Chest symptoms*	26 (38%)	Chest signs [#]	12 (17%)
Weight loss	24 (35%)	Jaundice	10 (14%)
Diarrhoea	16 (23%)	Confusion	2 (3%)
Jaundice	6 (7%)	Mild ascites	1 (1%)

*Cough, chest pain, shortness of breath. [#]Consolidation, crepitations.

Table 2 Haematology and biochemistry on the day of admission in 69 patients with liver abscess

Test	Median (range)	Normal	Abnormal test result <i>n</i> (%)
ALT (U/l)	49 (2–400)	7–33	46 (67%)
AST (U/l)	42 (9–545)	10–34	34 (49%)
ALP (U/l)	472 (112–2,005)	60–306	44 (64%)
Bilirubin (µmol/l)	15 (4–456)	2–20	25 (36%)
Haemoglobin (men) (g/l)	11.7 (7–15.1)	131–166	29 (74%)
Haemoglobin (women) (g/l)	11.15 (5.7–13.6)	110–146	14 (47%)
White cell count ($\times 10^9/l$)	17.3 (2.5–34.9)	3.5–9.5	61 (88%)
Neutrophilia ($\times 10^9/l$)	14.49 (1.46–33.26)	1.7–6.5	62 (90%)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase.

Table 3 Underlying pathology in 65 patients with pyogenic liver abscess

Cause	Comment	<i>n</i> (%)
Biliary	Three had recent trauma	18 (28%)
Portal	Three were diabetic	31 (48%)
Cryptogenic		4 (6%)
Not investigated		12 (18%)
Total		65 (100%)

Pyogenic liver abscess

A potential underlying disease for PLA was found in 49 patients (75%) of those with PLA and in 92% of those investigated for underlying pathology (Table 3). Spread of infection via the portal venous system was more frequent in patients aged ≥ 60 years ($p=0.019$). Biliary tract abnormality was equally common in both age groups. One patient

in the cryptogenic group was diagnosed with large bowel cancer two years after his recovery from PLA (normal barium enema at time of PLA). In 21 patients with PLA, a diagnosis of underlying disease was made as a result of investigations conducted after the PLA had been identified. These included diverticular disease in 13 (including abscesses and/or fistulae), four with inflammatory bowel disease (2 colitis, 2 Crohn's disease), one gall-bladder cancer and one colonic cancer, one with a chicken bone penetrating the gastric wall, and one with a track between a peptic ulcer and the LA.

Thirty-eight patients (58%) with PLA had a single abscess; 27 (42%) had multiple abscesses. Abscess formation was in the right lobe in 43 (66%), the left lobe in 5 (8%) and both lobes in 17 (26%). There were no differences in the causative bacterial agent in patients with single and multiple PLAs. Radiological findings are summarized in Table 4.

A microbial pathogen was isolated in 51 patients (78%, Table 5). The source of isolates was blood in

Table 4 Radiological findings in 69 patients with liver abscess

Type of imaging		Number	%
Chest X-ray	Total	42	61
	Abnormal	14/42	33
	Elevated right hemidiaphragm	2	
	Pleural effusion (2 left, 2 right)	4	
	Consolidation right base	4	
	Atelectasis right lower lobe	1	
	Others	3	
Abnormal X-ray	Total	21	30
	Abnormal	5/21	24
Ultrasound	Enlarged spleen, Biliary stent, Calcifications, Elevated right hemidiaphragm		
	Total	67	97
	Not suspicious of liver abscess	7/67	10
Abdominal CT	Suspicious of liver abscess	60/67	90
	Total	18	26
	Abnormal	18/18	100

Table 5 Bacterial isolates in 51 patients with pyogenic liver abscess

Bacteria	<i>n</i>	Isolated from pus (<i>n</i>)
Gram-negative bacilli (total)	23	16
<i>Escherichia coli</i>	11	9
<i>Pseudomonas</i> spp.	3	2
<i>Klebsiella ozaenae</i>	1	0
<i>Morganella morgani</i>	1	1
Coliforms (not speciated)	7	4
Anaerobes (total)	13	9
<i>Bacteroides</i> spp.	8	6
<i>Fusobacterium</i> spp.	2	0
Others	3	3
Streptococci (total)	31	23
<i>Streptococcus milleri</i>	17	12
α -Haemolytic <i>Streptococcus</i>	5	4
<i>Enterococcus</i>	5	5
<i>Streptococcus pneumonia</i>	2	1
Others	2	1
<i>Staphylococcus aureus</i> (total)	2	2
Total	72	50

12 patients (24%), pus in 26 (51%), and both in 13 (25%). 14 patients had negative cultures, of whom two had Gram-negative bacteria seen on a Gram film of pus but were subsequently culture-negative. More than one organism was isolated in 25% of the patients with a positive culture.

The treatment regimens used are shown in Table 6. All patients received anti-microbial therapy. There was no change in the pattern of management over the study period.

Seven patients with PLA had eight recurrences: five had malignancy, one with granulomatous disease had two recurrences, and one had hyper-IgE syndrome. Five patients who had recurrences underwent percutaneous needle aspiration (PNA) (one died). A further two had percutaneous catheter drainage (PCD), and one required surgery. Six out of eight had multiple lesions ($p = \text{NS}$). The main predictor of recurrence was underlying malignancy (OR 21.6, 95%CI 3–113.9). There was no association with gender, microbial isolates, duration of antimicrobial therapy, duration of hospital admission or delay in making the diagnosis. One patient died (underlying malignancy) and six made a full recovery.

Eight deaths with PLA in this series were recorded, one following relapse. The overall case fatality in PLA was 12.3%. The gender distribution was equal. The median age of the death was 67 years (range 56–86). Factors associated with

Table 6 Type of treatment and outcome in 65 patients with pyogenic liver abscess

Treatment method	<i>n</i>	Mean \pm SD hospital stay (days)	Death
Antibiotic alone	12	27 \pm 15	5
Antibiotic and procedure	43		
PNA	24	26 \pm 12	1
PCD	11	20 \pm 12	1
PNA and PCD	8	23 \pm 10	
Surgery/PCD/PNA	10	27 \pm 16	
Surgery and PNA	1		
Surgery and PCD	1		
Surgery and PCD and PNA	1		
Surgery alone	7		1
Total	65		8

PNA, percutaneous needle aspiration; PCD: percutaneous catheter drainage.

increase case fatality were underlying malignancy (OR 14.1, 95%CI 1.8–49.7), and shorter duration of antimicrobial therapy (average 18.7 vs. 39.8 days; $p = 0.004$), though this was probably because of premature death while on treatment. There was no significant association with age, multiple lesions, gender, days of hospital admission, or delay in making the diagnosis in this series.

Amoebic liver abscess

Four patients had positive *Entamoeba histolytica* serology. A history of foreign travel was documented in 14 (20%) of all the patients with LA. All patients with positive *Entamoeba histolytica* serology had travelled to endemic areas. Three had single lesions; one had multiple lesions. All lesions were in the right lobe. All were treated with broad-spectrum antimicrobials including metronidazole; two had PCA and two had PCD. No deaths were recorded, but one had recurrence that required further drainage, later making a full recovery.

Discussion

The crude annual incidence rate of LA in this series is higher than the figures reported in other studies of ~5–13 cases/100 000 admissions.^{6,14,18,19} The findings reported here may reflect a real increase in incidence as this series is not based upon

experience in a tertiary referral centre and none of the patients had had organ transplantation, were cirrhotic or known to be HIV-infected. It is also likely that we have missed some cases. On the other hand, the increase in incidence may be partly an artifact resulting from improvements in diagnosis. The upward shift in age range has been demonstrated in earlier reports,^{8,9,14,17,18,20} but is more marked in this series, with 77% of cases aged over 50 years. This contrasts markedly with the pre-antibiotic era study by Oschner *et al.*,⁷ where median age was the third decade in the setting of intra-abdominal infections (commonly appendicitis).

The most common underlying pathophysiological mechanism in this series was spread of infection via the hepatic portal vein. Our data accord with two previous reports^{1,9} and contrast with other studies that suggested that either biliary spread²⁻⁷ or cryptogenic aetiology was most common.^{3,4,8} The higher incidence of portal spread in patients aged > 60 years ($p=0.019$) probably reflects age-related increases in diverticular disease and bowel malignancy. On the other hand, atrophic gastritis associated with loss of peptic acid production is also more common in the elderly, and results in changes in bowel bacterial flora.²¹ The loss of gastric acid may therefore increase the risk for contracting bacterial infections and PLA.²²⁻²⁵ In this series, one patient out of four with cryptogenic liver abscess was subsequently diagnosed as having colonic cancer two years later despite having had a normal barium enema at the time of the PLA. None of the patients in this series had cirrhosis, which increases the risk of LA.²⁶

Although plain abdominal radiographs were seldom of diagnostic benefit, 79% of patients who had pulmonary pathology on the chest radiograph, had changes at the right base, emphasizing the maxim that LA must be considered in the differential diagnosis of right-sided pulmonary parenchymal and/or pleural findings, in accordance with previous reports.^{8,27} Abdominal US was sensitive and specific in 90% in this series, and in those who had CT scanning this was positive in 100%, but was not routinely used. In this study, the number of PLAs located in the left lobe alone was 8%, a rate similar to a previous report.¹⁰ The variations in location and multiplicity of abscesses may be explained by improved diagnostic techniques and skills. The present study did not find any correlation between the presence of either single or multiple lesions and underlying disease.

A microbial pathogen was most commonly found when pus was obtained and cultured. Polymicrobial cultures were noted in 16% of

blood cultures, while abscess pus cultures were polymicrobial in 33%. It is important when interpreting the results of blood cultures to recognize that they may not fully reflect the microbial contents of the abscess. This series contrasts with previous reports^{10,19} that suggested that prognosis was proportional to the number of isolates in the blood (case fatality being higher in those with two or more isolates)—in none of the eight patients who died in this series was polymicrobial infection detected. This may perhaps reflect the absence of immunocompromised patients in this series.

All patients received broad-spectrum antibiotics, which were given for a mean of 37 days. The use of antibiotics alone is controversial; success rates as high as 79%²⁰ and as low as 7%²⁸ having been reported. In this series, the success rate of antibiotics alone was 58.4% (7/12): five of the patients who had other underlying life-threatening diseases died, but no recurrence was recorded in the seven patients who recovered.

Before and during the 1970s, surgical drainage was considered the treatment of choice for LA.^{1,10,19} However, this view has changed over time, and PCD and PNA have been shown to be as effective as open surgical therapy.¹³⁻¹⁵ Overall, in this series, PCD/PNA via an interventional radiological approach was extremely successful as initial treatment. While the percutaneous approach appeared to be more successful than surgery in achieving cure (10% vs. 14%) and reducing case fatality (4% vs. 14%), only seven patients had surgery as initial procedure and the data may represent a selection bias, as some patients who underwent surgery were deemed unsuitable for the less invasive procedures. When surgery was used following the percutaneous approach, it was successful on all occasions. The type of treatment (PNA/PCD) chosen may have been influenced by several factors (e.g. size of LA, multiple LAs, clinician/radiologist's decision and others). Where skilled interventional radiology is available, these data offer some support for the use of PCD/PCA as primary treatment in patients with either single or multiple LA, although it is hard to draw definite conclusions. All patients who had surgical intervention had a single liver abscess, and several factors such as the presentation (acute abdomen), underlying pathology and failure of other treatment modalities may have influenced this choice of therapy.

The case fatality rate in the present series was 12.3%, lower than the figures of 19–50% reported in some previous studies.^{6,10,12,18,26} While earlier presentation, diagnosis, and treatment are likely to be associated with improved survival,^{4,7,12,19,26} the

most important determinants of case fatality in the present series was the presence of underlying malignancy. Patients with biliary tract disease had the worst survival of any group, with a case fatality rate of 33%. By contrast, the case fatality rate in patients with portal spread was 6%, while no deaths were recorded in the cryptogenic group or in patients who had not been investigated for underlying pathology. This may reflect the possibility that these patients had less severe (or no) underlying disease.

Although we acknowledge the limitations of retrospective studies, this series represents a 10-year experience of liver abscess in a single UK centre. The clinical presentation of patients with LA was variable, although the most common symptoms and signs related to fever and abdominal pain/tenderness. The most commonly associated pathology was portal tract disease. Searching for associated pathology is an integral part of management, and the diagnosis of cryptogenic liver abscess should only be made after aggressive investigation, particularly of the gastrointestinal tract. We recommend US as the initial diagnostic investigation, and percutaneous drainage or aspiration plus antibiotic(s) as first-line treatment. The prognosis of LA has improved with time, and death is now rare except in patients with malignant disease.

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