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Presentations of pyogenic liver abscess in one UK centre over a 15-year period

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ABSTRACT **Background and aim**: Pyogenic liver abscess (PLA) has been a condition of high mortality, improving over recent decades with combined antibiotic and percutaneous drainage. We aimed to identify the presenting features, diagnosis, microbiology, treatment and outcome for patients over a 15-year period at an inner-city hospital.
Methods: Patients with an appropriate discharge diagnosis were identified and case records retrospectively analysed.
Results: A total of 73 patient records were analysed. Common presenting features were anorexia, abdominal pain, fever, vomiting and weight loss with raised white cell count, C-reactive protein, alkaline phosphatase and hypo-albuminaemia. The delay following symptom onset to presentation was a mean of 17.3 days. The inclusion of PLA as a possible diagnosis on admission was only considered in 1% of cases. Positive blood or abscess culture was achieved in 63% of cases. We recorded a hospital mortality rate of 11%.
Conclusions: In this sample, PLA was rarely considered as a possible diagnosis at presentation. There are common presenting features, which should prompt early investigation. Our microbiological yield was lower than in some studies and may be due to the early empirical use of antibiotics, without microbiological guidance. Percutaneous drainage and antibiotic treatment remain the mainstay of management. The underlying cause for PLA is often not identified. Emerging septicaemia or underlying malignancy were strong predictors of mortality.

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INTRODUCTION

Pyogenic liver abscess (PLA) remains a condition associated with mortality, but in recent decades, with the advent of combined antibiotic therapy and percutaneous abscess drainage, the mortality has dropped from nearly 100% to 6–31%.[1] This combination has become the mainstay of treatment in most centres.[2] Incidence has been recently identified to be 3.6 per 100,000 population in one large American study,[3] but there is evidence of significant geographic variation, particularly in Far Eastern populations, where the incidence in Taiwan was recently estimated to be 17.6 per 100,000 population.[4] We wished to study the presentation patterns and outcomes of patients with PLA who presented in one multi-ethnic urban centre in the UK over a 15-year period.

METHODS

We searched the hospital's clinical coding database for all patients with the final diagnosis of 'liver abscess' or 'pyogenic liver abscess', between 1993 and 2008. The trust is a large teaching hospital serving a catchment population of about 500,000. The medical records were reviewed and data were extracted relating to patient demographics, medical history, presenting symptoms, initial investigations and working diagnosis on presentation. We also recorded the location of abscess, microbiology data, treatment and patient outcome.

RESULTS

A total of 86 patients were identified from the hospital database. Of these, 73 medical records were available to analyse. The remaining records were either not found (six) or no information relating to liver abscess was found in the record (seven). This may have been due to miscoding of the diagnosis and predominantly affected case notes from the early part of the study period. The false negative rate is unknown.

Patient demographics

A total of 53 patients (73%) were male and 20 female (27%). The mean age was 64.7 years (standard deviation, SD: 17; range: 21–93). Ethnically, 51 patients (70%) were Caucasian, 13 Asian (18%), five Chinese (7%) and four Afro-Caribbean (5%). Background medical problems identified included hypertension (12, 16%), ischaemic heart disease (6, 8%), diabetes mellitus (7, 10%) and bowel cancer (5, 7%). No previous medical problems were noted in 14 (19%) of patients.

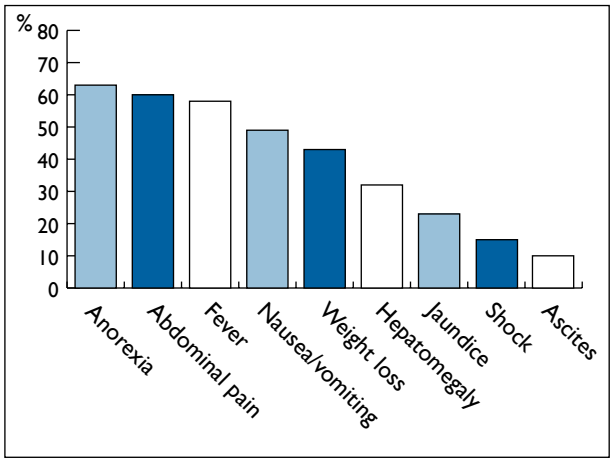

FIGURE 1 Percentage of patients with various clinical features on presentation.

Diagnosis

The average duration of symptoms prior to admission was 17.3 days (SD: 25.6; range: 1–168). Presenting features for patients with a subsequent diagnosis of PLA are shown in Figure 1 and initial laboratory data in Table 1.

Clinical evaluation of baseline chest radiograph was documented in 59 cases (81%). Thirty-five (59%) of these were normal, while nine (15%) showed a right-sided pleural effusion, six (10%) suggested consolidation and four (7%) suggested a raised right hemidiaphragm. Five showed other features: rib fractures (one), cardiomegaly (three) and radiographic signs of pulmonary oedema (one).

The initial diagnostic differentials formed by the admitting medical team varied widely. Liver abcess was the proposed admitting diagnosis in only one case (1%).

The mean time to diagnosis following admission was 4.4 days (SD: 3.6; range 0–19) and the method of confirmation of the diagnosis was by abdominal ultrasound in 56 patients (77%), computed tomography (CT) in 12 (16%), ultrasound and computed tomography in four (5%) and by exploratory laparotomy in one (1%). Abscesses were confined to the right hepatic lobe in 54 (74%), the left lobe in 12 (16%) and in both lobes in seven (10%). There were solitary abscess in 49 (67%) of patients, two abscesses in eight (11%) and three or more in 16 (22%).

Microbiology

Blood cultures were recorded as taken from 66 patients (90%). The mean time for taking samples was on day 2.6 of admission (SD: 2.95; range 1–22). Abscess culture (via percutaneous aspiration) was documented in 71 cases (97%). Two patients had positive blood cultures in the presence of advanced malignancy and percutaneous sampling or drainage was deemed clinically inappropriate. The mean time from admission to obtaining culture specimens was 6.7 days (SD: 5.7; range 2–27). A total of 61 (84%) had both blood and abscess culture. One patient had neither blood nor abscess culture due to advanced malignancy. Microbiological data are shown in Table 2.

The overall microbiological yield for patients who had blood or abscess culture was 63%. Twenty-four patients grew no organisms from blood or abscess and, within this group, the mean duration from starting antibiotics

TABLE 1 Laboratory data

Parameter	Mean value	Standard deviation	Percentage with abnormal value
Haemoglobin (g/dl) n=73	11.18	2.0	<10 g/dl 19
White cell count (10^9/l) n=73	19.8	7.5	>10 x 10^9/l 93
C-reactive protein (mg/l) n=45	267	125	>10 mg/l 100
Bilirubin (µmol/l) n=73	29.2	31.8	>22 µmol/l 38
Alanine transaminase (U/l) n=73	94.1	72.1	>60 U/l 63
Alkaline phosphatase (U/l) n=73	378.4	249.8	>145 U/l 85
Albumin (g/l) n=73	29.2	4.6	<35 g/l 95

TABLE 2 Microbiology data

Positive organism in blood or abscess fluid n=72	Positive blood cultures n=66	Positive abscess culture n=71	Both positive (same organism) n=61	Both positive (different/ additional organism) n=61	Both negative n=61
45 (63%)	25 (38%)	43 (61%)	10 (16%)	6 (10%)	24 (39%)

Organism	**Frequency (percentage)** n=51
Gram-positive aerobes	
Streptococcus milleri	6 (12%)
Other *Streptococcus* spp.	6 (12%)
Streptococcus intermedius	5 (10%)
Haemolytic *Streptococcus* group G	3 (6%)
Enterococcus faecium	3 (6%)
Staphylococcus aureus	2 (4%)
Methicillin-resistant S. aureus	2 (4%)
Enterococcus faecalis	2 (4%)
Gram-negative aerobes	
Escherichia coli	12 (24%)
Klebsiella spp.	5 (10%)
Gram-negative anaerobes	
Bacteroides spp.	5 (10%)

to taking blood culture was 1.1 days (SD: 1.2; range: 1–4). The mean duration from starting antibiotics to obtaining abscess culture was 5.1 days (SD: 5.4; range 1–21). A total of 51 organisms were isolated in 45 patients.

Management

Antibiotic therapy

A total of 72 patients (99%) received intravenous followed by oral antibiotics. One patient received palliative care only. Seventeen patients (24%) received first-line antibiotics only, lasting for a mean of 25.5 days (SD: 20.6; range 3–56). Thirty-three patients (46%) were changed to second-line antibiotics with a mean total antibiotic treatment of 26.1 days (SD:15.2; range 5–62). Twenty-two (31%) were changed on to third-line antimicrobials and underwent a mean treatment duration of 33.3 days (SD: 24.1; range 3–118). First-line antibiotic treatment was based on a third-generation cephalosporin plus anti-anaerobic treatment in 53 patients (74%). A penicillin with anti-anaerobic treatment was used in 14 cases (19%). The remaining antimicrobial choices represented a range of alternative diagnoses on admission such as presumed urinary tract infection (three patients) and/or non specific cellulitis (two patients). Second- and third-line antibiotics were prescribed based on culture results or local microbiological advice.

Percutaneous drainage

Percutaneous abscess drainage was performed on 66 patients (90%). Reasons for not draining abscess included patients with advanced malignancy or due to technical difficulties such as the small size or location of multiple abscesses. The mean time from admission to drainage (where undertaken) was 9.5 days (SD:7.2; range 2–28).

Aetiology

The underlying aetiology for PLA was unclear in 35 cases (48%). Benign bowel conditions (diverticulosis, Crohn's disease or appendicitis) were implicated in six cases (8%) and malignant conditions in five (7%). Benign biliary tract pathology (gall stones, cholangitis, post-endoscopic retrograde cholangiopancreatography [ERCP]) were deemed the most likely cause in 17 cases (23%) and malignant biliary tract disease in nine (12%). One patient (1%) was thought to have developed PLA due to perforated duodenal ulcer.

Complications

A total of 22 (30%) of patients developed a pleural effusion during admission, six (8%) developed ascites and 18 (25%) had evidence of significant bacteraemia (hypotension and fever).

Outcome

The mean duration of hospitalisation was 26.8 days (SD: 24.1; range: 4–186). Sixty patients (82%) were discharged home alive, five (7%) were transferred to another care facility and eight (11%) died during the index admission.

TABLE 3 Prognostic factors associated with death

Factor	Number alive	Number dead	Mortality (%)
Age			
>60	44	6	12
≤60	21	2	8.7
Medical history			
Diabetes	5	2	29
Hypertension	8	4	33
Ischaemic heart disease	4	2	33
Pancreatobiliary cancer	4	2	33
Bowel cancer	4	1	20
Culture (blood or abscess fluid)			
Positive	41	4	8.9
Negative	24	4	14.3
Abscess location			
Right lobe	47	7	13
Left lobe	11	1	8.3
Bilobar	7	0	0
Evidence of bacteraemia			
Yes	12	6	33
No	53	2	3.6
Admission haemoglobin			
> 10 g/dl	52	7	11.9
≤ 10 g/dl	13	1	7.1
Admission white cell count			
>10 x10^9/l	61	8	11.6
>20 x10^9/l	26	5	16.1
Admission serum bilirubin			
>22 µmol/l	24	4	14.3
≤22 µmol/l	41	4	8.9
Admission alkaline phosphatase			
>145 U/l	56	6	9.7
≤ 145 U/l	9	2	18.2
Admission serum albumin			
<35 g/l	62	7	10.1
≥35 g/l	3	1	25

The mean age of patients who died was 71.8 years (SD:11.4; range: 58–86). Two (25%) were female and six (75%) were male. Four (50%) had pre-existing hypertension, two (25%) had a malignancy (two pancreas, with one patient also having a bowel malignancy), two (25%) had ischaemic heart disease and two (25%) had diabetes. Four (50%) developed a presumed septicaemic shock state and one (13%) developed a nosocomial pneumonia and adult respiratory distress syndrome. All eight (100%) patients who died in hospital developed acute renal failure prior to death. The patients who died

following admission had a mean delay to hospital presentation of 12.2 days (SD: 7.9; range: 2–21). Possible prognostic factors associated with fatality using simple univariate analysis are shown in Table 3. A multifactorial analysis was not possible due to the small sample size.

DISCUSSION

The average age of patients in our sample of PLA was 65 years. This supports other series in demonstrating that the average age of patients who develop PLA has risen over recent decades, with an average presentation being in the sixth decade[5–11] or seventh decade.[1,12–16] As in previous studies, our patients were in general male.[1,3,5,6,8–10,12,14–16] Background medical history reflected conditions common in the aged population such as diabetes, hypertension and ischaemic heart disease.

There was a mean 'delay' of 17 days to admission following symptom onset and a further subsequent four-day mean delay until a diagnosis of PLA was considered/confirmed. This reflects the rather insidious and non-specific symptomatology that often occurs in PLA. The delay in the confirmation of the diagnosis following admission is of concern. Access to imaging has generally become easier over recent years, thus allowing rapid confirmation of liver abscess where the diagnosis has been considered or in cases where symptoms and signs are ambiguous. Reassuringly, we found little evidence that a delay in imaging (which has been a feature of other published series[1,14,17] as well as this cohort) affected mortality. Presenting symptoms in our study were typically multiple and non-specific, but commonly included anorexia, fever, nausea and abdominal pain. On physical examination hepatomegaly, jaundice and ascites were often recognised. The low index of suspicion of PLA may be due to this broad symptom clustering in our cohort.

Further clinical information from routine blood tests should suggest the possibility of PLA, particularly the presence of a raised white cell count, C-reactive protein, raised alkaline phosphatase and low albumin, as suggested by other series.[1,5,6,8,13,15] Baseline chest radiography often showed features that are retrospectively compatible with an associated PLA and diaphragmatic and/or pleural irritation/infection, but the confirmation of the diagnosis clearly relies on specific imaging of the liver. Most PLAs are reliably detectable by ultrasound imaging alone, but the increasing availability of CT – rather than any increase in sensitivity or specificity – is the most likely factor for the 16% in our cohort being diagnosed by this modality. It is also likely that patients with vague abdominal symptoms and no detected visceral abnormality on basic examination were often referred directly for CT to image other abdominal organs.

We confirmed the previous suggestion that PLAs are mostly confined to the right hepatic lobe,[1] which is likely to be the result of the portal venous anatomy. The right lobe also contains a denser network of bile canaliculi and accounts for more hepatic mass.

Abscess drainage has been shown to be beneficial in the treatment of PLA and percutaneous drainage is now standard practice.[3] Of our cohort, 97% underwent drainage. One of the main aims is to achieve a positive microbiological diagnosis to further guide antimicrobial management. Our overall microbiological yield, from blood and abscess culture, was 63%, which is low compared with other studies. A contributory factor to the low microbiological yield may be the early use of antibiotics in non-specific sepsis admission protocols. In our cohort, those with negative blood and abscess culture had received antibiotics, on average, one day prior to blood culture and five days before abscess culture, which will have affected culture yield, as a rapid sterilisation of blood cultures can occur within a few hours of the first antibiotic dose.[18] The validity of protocols mandating treatment without culture results is reasonable, but the absence of all blood cultures before treatment in this cohort was unusual.

We saw a typical microbiological spectrum which shows a preponderance of *Streptococcus* species. The other main isolates were *E. coli* and *Klebsiella* and *Bacteroides* species. This predominance of Gram-positive species is in contrast with studies from the Far East, where Gram-negative organisms such as *E. coli* and *Klebsiella* reliably top the diagnostic yield tables.[12,15] One possible explanation is that Gram-positive organisms are likely to be found in patients with infective sources which then spread to form secondary infection in the liver.[19] Furthermore, cultured organisms are likely to be different in Western urban settings compared with Eastern rural communities.

It is clear that there are patterns of antibiotic resistance, which are likely to increase in the setting of patients with indwelling biliary stents, recurrent cholangitis and multiple courses of antibiotics.[20] This factor is also important in relation to fungal super-infection. There are little formal data regarding the optimum duration of antibiotic therapy, but most units use a regimen of two weeks' parenteral treatment, followed by a more prolonged course (four to six weeks) of therapy, switching to oral antibiotics when clinical and inflammatory responses allow.[21] It was unclear in a number of our cohort how long oral antibiotic courses lasted, especially after discharge, hence our figures probably underestimate treatment duration.

As has previously been noted, we were unable to find an underlying cause for PLA in a substantial proportion of patients.[9] Where a source for PLA was identified, the biliary tract was the most commonly implicated structure. One study identified that ERCP was a useful modality in detecting the cause for PLA in patients where the

underlying diagnosis was not clear[15] and may have detected abnormalities in some of the 48% of our cohort where the aetiology was undetermined. Further clarification of the aetiology of our 'cryptogenic' cases with colonoscopy and ERCP may have improved the identification of underlying lesions.[9]

The in-hospital mortality rate for this small series was 11%. Until the late 1980s the overall mortality rate of PLA remained high at 40%,[22] improving with better imaging, more effective use of antibiotics and the trend towards abscess drainage to more contemporary mortality rates of 10–25%.[13] Older age (>60 years) and the presence of significant co-morbidity were features associated with higher mortality. Emerging septicaemia and shock was an ominous factor in our cohort and the presence of malignancy was also a predictor of in-hospital death. We could not make a detailed statistical analysis from our small sample. However, there are some interesting features in this cohort such as those with negative cultures, normal albumin, low alkaline phosphatase and higher haemoglobin apparently being associated with lower mortality. The validity of these associations could only be established with a larger cohort and by multifactorial analysis to exclude confounding associations.

We suggest that with a heightened suspicion for PLA, early radiological diagnosis and subsequent drainage can be performed, and by waiting for culture results in the non-septic patient, targeted antimicrobials can be prescribed, thus reducing antibiotic-associated complications and drug resistance. The continuing potential for evolving severe sepsis should be noted, actively monitored and treated aggressively where it emerges.

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