Liver abscess presentation and management in Saudi Arabia and the United Kingdom

Ali Albenmousa, Faisal M. Sanai, Amit Singhal, Mohammed A. Babatin, Adnan A. AlZanbagi, Malfi M. Al-Otaibi, Altaf H. Khan, Khalid I. Bzeizia

From the aDepartment of Medicine, Division of Gastroenterology and Hepatology, and bTotal Quality Management, Riyadh Military Hospital, Riyadh, Saudi Arabia; cIntegrated Department of Gastroenterology, Bradford Teaching Hospitals National Health Service Trust, United Kingdom; dKing Fahad General Hospital, Jeddah, Saudi Arabia

Correspondence: Dr. Faisal Sanai · Division of Gastroenterology and Hepatology (A41), Department of Medicine, Riyadh Military Hospital, PO Box 7897, Riyadh 11159, Saudi Arabia · F: +966 1 4757859 · fsanai@rmh.med.sa · Accepted: December 2010

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BACKGROUND AND OBJECTIVES: Liver abscess (LA) is a well-described disease in the medical literature; however, information about its characteristics and outcome in the Middle East is lacking. We compared the mode of presentation, risk factors, management and outcome of LA patients in Saudi Arabia with cases from the United Kingdom (UK).

DESIGN AND SETTING: Retrospective review of LA patients from three tertiary care centers (2 from Saudi Arabia and 1 from the UK) over a period of 10 years, from 1995 to 2005.

PATIENTS AND METHODS: Data collected included demographic characteristics; clinical presentation; biochemical, microbiological and radiological findings; treatment modalities; and outcome.

RESULTS: A total of 83 patients were diagnosed with LA, including 48 patients from Saudi Arabia and 35 patients from the UK. The mean (SD) age was 45.2 (20.3) years for those from Saudi Arabia and 55.4 (18.8) years for those from the UK (P=.022). The majority of the patients were males (70% from Saudi Arabia and 80% from the UK). Upper abdominal pain and fever were the commonest symptoms, each reported in 87% of the cases. Alkaline phosphatase elevation was the commonest liver function abnormality, seen in 66 (80%) patients. Organisms were isolated in 43 (52%) cases and the majority of these were coliforms (58%). Amebic liver abscesses occurred in 19 (23%) patients and all of those patients were either from or had traveled recently to the Indian subcontinent. Complete resolution of the abscesses was achieved in 66 (80%) patients with aspiration and/or antibiotics, and 9 (10.8%) patients died. On multivariate analysis, underlying malignancy, hypotension and chest signs at presentation were predictors of poor outcome (P=.008, .029 and .001, respectively).

CONCLUSIONS: Successful resolution of LA is achievable in the majority of the cases, although underlying malignancy is associated with poor outcome. Amebic liver abscesses must be considered in patients with a history of travel to endemic areas.
port the mode of presentation of LA, risk factors, management and outcome in two medical centers in Saudi Arabia and compare them to a group of patients diagnosed with LA in the UK over a similar time period.

PATIENTS AND METHODS

We conducted a retrospective analysis of medical records for all patients diagnosed with LAs from three medical centers (Riyadh Military Hospital and King Fahad General Hospital, Saudi Arabia; and Bradford University Hospital, UK) during the period from January 1995 to January 2005. Cases were identified by searching individual hospital databases. The study was performed in accordance with the declaration of Helsinki. The study was approved by the institutional ethical committees of all participating centers.

Diagnosis of PLA was based on typical appearance on ultrasound (US) or computed tomography (CT) of abdomen with clinical features consistent with the diagnosis; and/or US or CT-guided aspiration of pus from a hepatic lesion. ALA was diagnosed based on a positive indirect hemeagglutination antibody titer equal to or greater than 1:64 in the presence of LA on US or CT scan examination. Charts were abstracted to a data collection form. Data collected included age, gender, ethnicity, underlying medical conditions, symptoms, signs, biochemical and hematological tests, radiological imaging (including chest radiographs, abdominal US/CT) and microbiological features. Complications and outcome after intervention were recorded. The study protocol was approved by the Medical Ethics Committee in all three centers.

Statistical analysis was performed with SPSS 17 (SPSS Inc., Chicago, IL, USA). For categorical variables, we used a chi-square or Fisher exact test, as appropriate; and for continuous variables, the t test was applied to compare means. Multivariate analysis was then done for statistically significant variables from univariate analysis, using binary logistic regression model. Results were considered statistically significant if the P value was <.05.

RESULTS

Eighty-three patients were diagnosed with LAs, 48 patients from Saudi Arabia and 35 patients from the UK. The mean (standard deviation) age was 49.5 (20.2) years (range, 1-95 years); of these patients, 55 (66.3%) patients were <60 years old. The mean age was 45.2 (20.3) years for patients from Saudi Arabia and 55.4 (18.8) years for those from the UK (P=.022) (Table 1). Sixty-two (74.7%) patients were males for a male:female ratio of 3:1 with similar gender distribution among both groups. Thirty-five (42%) patients were of Saudi origin, 21 (25.3%) were Caucasian, 15 (18%) were from South Asia, and 12 (15%) were Chinese and Afro-Caribbean. The mean duration to diagnosis was 23.3 (25.2) days (range, 1-150 days). The mean time needed to diagnosis was relatively shorter in patients from the UK (6.1 vs. 7.5 days), but this did not reach statistical significance (Table 1). Upper abdominal pain and fever were the commonest symptoms, occurring in 88.0% and 86.7% of the patients, respectively. The frequency of other symptoms are listed in Table 2. During clinical examination, fever and abdominal tenderness were the most common findings, reported in 68 (82%) patients. Hepatomegaly was present in 34 (41%) patients, while jaundice was noticed in 9 (11%) patients only. Septic shock and hypotension developed in 10 patients. Results of chest examination were reported to be abnormal in one quarter of the patients (Table 2). White blood cells were elevated in 44 (53%) and bilirubin in 17 (21%) of the cases. Alkaline phosphatase elevation was the commonest liver function abnormality, seen in 66 (80%) patients. Unilateral pleural effusion was a frequent finding on chest x-ray, occurring in 20% of the patients.

The abscesses were multiloculated in 29 (35%) patients; and the right lobe was the commonest site affected, 58 (70% of the cases) compared to 17 (20%) in the left lobe. Abscesses were found in both lobes in 8 (10%) patients. Location of abscess and the presence of multiloculation did not influence the outcome (Table 3). Sixty-five patients required drainage of abscess during their disease course. Organisms were isolated in 43 (52%) cases; majority were coliforms (49%), and these

| Variable                  | Saudi Arabia (n=48) | United Kingdom (n=35) | P value |
|---------------------------|---------------------|-----------------------|---------|
| Age (years)               | 45.2 (20.3)         | 55.4 (18.8)           | .022    |
| Male sex (%)              | 34 (70.8)           | 28 (80)               | .246    |
| Time to diagnosis (days)  | 7.5 (7.7)           | 6.1 (6.8)             | .408    |
| Amebic abscess (%)        | 10 (20.8)           | 9 (25.7)              | .548    |
| Diabetes mellitus (%)     | 9 (18.8)            | 9 (25.7)              | .237    |
| Underlying malignancy (%) | 4 (8.3)             | 5 (14.3)              | .304    |
| Abscess drainage (%)      | 42 (87.5)           | 23 (65.7)             | .018    |
| Complete resolution (%)   | 36 (75)             | 30 (85.7)             | .027    |
| Death (%)                 | 5 (10.4)            | 4 (11.4)              | .577    |

Data expressed as mean (SD) or n (%).
included *Klebsiella* spp (10 patients), *E coli* (8 patients) and mixed coliforms (3 patients). *Streptococcus milleri* was found in 6 patients, *Pseudomonas* in 4 patients, *Staphylococcus aureus* in 2 patients and coagulase-negative staphylococcus in 2 patients. Anaerobes were isolated from 2 patients, while tuberculous LA was found in 1 patient (Figure 1). Blood culture was positive in 24 (29%) patients; and in one third of them, *Klebsiella* was isolated. Amoebic serology was positive in 19 (23%) patients; all were either from or had traveled recently to the Indian subcontinent, and these patients were considered to have ALA. Hydatid serology was done in 41 patients and was positive in 1; however, the radiological appearance was not consistent with hydatid cyst. *Entamoeba histolytica* was not identified in any of the cases after drainage, including those with positive serology. The outcome of patients with ALA was not significantly different when compared to that of patients with PLA ($P$=.284). Predisposing conditions in the form of intra-abdominal sepsis was found in 11 (17%) patients, including diverticular disease, hepatic trauma, recurrent cholangitis, appendicular abscess and post-endoscopic retrograde cholangiopancreatography status.

Complete resolution of the abscesses was achieved in 66 (80%) patients with aspiration and/or antibiotics. Nine (10.8%) patients died. Complications occurred in 6 patients—3 had rupture of the abscess, 2 had recurrence and fistula developed in 1 patient. Resection of a liver lobe or the abscess was required in 3 (4.6%) patients.

Underlying malignancy was the most important prognostic factor associated with half of the deaths in this series ($P<.0001$) (Table 4). Among other variables tested in univariate analysis, chest signs and hypotension at presentation were significant predictors of death ($P=.001$, $P=.042$, respectively), as well as elevated levels of ALT and bilirubin as previously mentioned (Table 4). On multivariate analysis, underlying malignancy, hypotension and chest signs at presentation were found to be independent predictors of mortality ($P=.001$, $P=.008$ and .029, respectively) (Table 5). On the other hand, both hypotension and chest signs at presentation had a negative impact on resolution of the abscess ($P=.028$ and .048, respectively); but on multivariate analysis, only hypotension ($P=.047$) was associated with nonresolution of abscess. Diabetes was present in 13 (20%) patients and was associated with increased mortality in patients from Saudi Arabia ($P=.039$) but not in those from the UK ($P=.357$).

**DISCUSSION**

Although rare, LA is still an important clinical condition.

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**Table 2.** Frequency of symptoms and signs in 83 liver abscess patients.

| Symptoms                  | All patients | Saudi Arabia | United Kingdom | $P$ value |
|---------------------------|--------------|--------------|----------------|-----------|
| Fever                     | 72 (87)      | 43 (89.6)    | 29 (82.9)      | .372      |
| Abdominal pain            | 73 (88)      | 41 (85.4)    | 32 (91.4)      | .214      |
| Nausea/Vomiting           | 38 (46)      | 20 (41.7)    | 18 (51.4)      | .313      |
| Diarrhea                  | 12 (15)      | 6 (12.5)     | 6 (17.1)       | .516      |
| Chest pain                | 11 (13)      | 2 (4.2)      | 9 (25.7)       | .006      |
| Cough                     | 8 (10)       | 5 (10.4)     | 3 (8.6)        | .561      |
| Shortness of breath       | 7 (8)        | 2 (4.2)      | 5 (14.3)       | .094      |
| Rigor and night sweating | 14 (17)      | 9 (18.8)     | 5 (14.3)       | .457      |
| Weight loss               | 22 (27)      | 9 (18.8)     | 13 (37.1)      | .044      |

| Signs                     | All patients | Saudi Arabia | United Kingdom | $P$ value |
|---------------------------|--------------|--------------|----------------|-----------|
| Abdominal tenderness      | 68 (82)      | 37 (77.1)    | 31 (86.8)      | .179      |
| Pyrexia                   | 68 (82)      | 39 (81.3)    | 29 (82.9)      | .632      |
| Hepatomegaly              | 34 (41)      | 23 (47.9)    | 11 (31.4)      | .118      |
| Chest signs               | 19 (23)      | 12 (25.0)    | 7 (20.0)       | .424      |
| Hypotension/shock         | 10 (12)      | 8 (16.7)     | 2 (5.7%)       | .139      |
| Jaundice                  | 9 (11)       | -            | -              | -         |

| Parameter                 | All patients | Saudi Arabia | United Kingdom | $P$ value |
|---------------------------|--------------|--------------|----------------|-----------|
| Leukocytosis              | 19.4 (13.3)  | 18.8 (13.8)  | 21.6 (11.4)    | .525      |
| Hyperbilirubinemia        | 27.7 (44.0)  | 27.5 (46.1)  | 30.8 (6.4)     | .888      |
| Raised alanine transaminase| 94.1 (144.2) | 89.5 (163.2) | 107.5 (68.1)   | .691      |
| Raised alkaline phosphatase| 488.0 (291.4) | 422.0 (281.6) | 604.3 (276.6)  | .011      |

| Right lobe (%) | 52 (62.7) | 28 (58.3) | 24 (68.6) | .184 |
| Left lobe (%)  | 18 (21.7) | 13 (27.1) | 5 (14.3)  | .144 |
| Both lobes (%) | 8 (9.6)   | 4 (8.3)   | 4 (11.4)  | .468 |
| Multiloculated | 29 (34.9) | 19 (39.6) | 10 (28.6) | .211 |

| Chest x-ray | Consolidation (%) | 5 (6) | 1 (2.1) | 4 (11.4) | .098 |
| Effusion (%) | 16 (19) | 11 (22.9) | 5 (14.3) | .243 |
| Raised hemidiaphragm (%) | 8 (10) | 4 (8.3) | 4 (11.4) | .456 |
It requires a high index of suspicion for diagnosis since many patients may not present with a typical history and clinical findings. In this series, 15% of the patients did not manifest fever and abdominal pain at presentation; and adding to this the overlap of symptoms with other conditions like cholecystitis and hepatitis, the diagnosis of LA might be a clinical challenge. It is a potentially life-threatening condition with a mortality rate ranging between 10% and 40%. Reduction in mortality rates has been consistently observed over the last three decades. One tenth of the patients in this series have died during disease course, and although this is considered relatively low, some studies have reported mortality rates as low as 6%. An important observation in this study, consistent with that in earlier reports, is that mortality was related to the presence of other major comorbidities like advanced underlying malignancy in majority of the cases. The combination of LA and malignancy, hepatopancreatic in particular, carries a grave prognosis; and despite relatively good response to the initial management, with a 20% in-hospital mortality, more than 70% of these patients die within 6 months secondary to progression of their underlying malignancy.

Age has frequently been reported as a predictor of mortality, especially in developed countries, as seen in our series; however, this finding was not observed in the patients from Saudi Arabia. One possible explanation is the tendency of LA to occur at younger ages in developing countries. The other poor prognostic factor found in this analysis is respiratory compromise at presentation in the form of pleural effusion and lung consolidation, which despite being commonly described with ALA in particular, has not been linked to a worse outcome. This finding was more obvious in patients from Saudi Arabia, but was consistent when all patients were included in the analysis. It would therefore be prudent to include imaging of the chest as part of initial evaluation of LA, along with monitoring of respiratory symptoms during follow-up of these patients.

Several risk factors for the development of PLA have been reported from large-population studies. Diabetes mellitus is the most important risk factor, with a 3.6-fold increased risk. Additionally patients with PLA with diabetes had a higher 30-day post-discharge mortality rate compared with patients with PLA who were not diabetic. Twenty percent of patients in this series were diabetic, but the association with overall mortality was not observed, possibly because of the small sample size and the low event rate. Nevertheless, a statistically significant correlation with mortality was found in the Saudi population. Other previously reported risk factors for PLA, including liver cirrhosis (alcoholic in particular) together with several congenital and acquired immunodeficiency states (common variable immunodeficiency, congenital hypogammaglobulinemia, and systemic immunosuppression), which commonly result in infection with unusual organisms have been seen at a very low rate in this group of patients.

Entamoeba histolytica is an important health risk.
to travelers in endemic areas. We made the diagnosis of ALA serologically,\(^\text{18}\) and we were not able to demonstrate *E histolytica* cysts in any aspirate. The clinical outcome of ALA did not differ significantly when compared to that of PLA in both groups. As expected, more drainage procedures were required in PLA (85% vs. 63% in ALA) since most of the ALA patients respond well to antimicrobial agents,\(^\text{19}\) yet this was not statistically significant (\(P=0.069\)). Although this study was not designed to look at this outcome specifically (drainage vs. no drainage for ALA), it serves to add to the ongoing debate in the medical literature about this approach.\(^\text{20}\)

In conclusion, our study has demonstrated some differences in the mode of presentation of LA and the effect of various risk factors in different geographical parts of the world although outcome and management were similar. A small sample size is a major limitation of the study, and therefore we encourage better reporting of this condition through a nationwide database search to further clarify the risk factors and microbiological spectrum, which in turn may influence the management and outcome of disease.

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