

CHARACTERISTICS OF UNDIAGNOSED LIVER ABSCESES ON INITIAL PRESENTATION AT AN EMERGENCY DEPARTMENT

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Liver abscesses often present with nonspecific symptoms and laboratory examination abnormalities, resulting in missed diagnoses at emergency departments (ED). The purpose of this study was to determine if there are differences in presentation and prognosis between patients in whom liver abscess is diagnosed at an ED or once the patient has been transferred to a ward. Patients with a liver abscess who were discharged from our hospital between 2005 and 2007 were retrospectively reviewed. We compared the clinical characteristics between patients with liver abscess diagnosed at an ED or in a ward. Patients with liver abscess diagnosed at an ED had more abdominal pain (73.4% vs. 42.9%, $p < 0.001$), longer duration of symptoms before hospitalization (5.5 days vs. 3.8 days, $p = 0.034$) and fewer respiratory tract symptoms (12.5% vs. 24.5%, $p = 0.05$). Fewer cases with abnormal chest X-rays also existed for these patients (4.7% vs. 14.7%, $p = 0.048$). Cases not diagnosed at ED had delayed diagnoses for 4.41 ± 3.16 days. Rates of mortality (6.3% vs. 8.2%, $p = 0.740$), shock (19.5% vs. 20.4%, $p = 0.896$), and length of hospital stay (19.6 days vs. 22.4 days, $p = 0.173$) were not significantly different between the patients diagnosed at an ED and those diagnosed later in a ward. Most information collected at the ED could not be used to aid diagnosis. Only abdominal pain was highly associated with liver abscess diagnosed at the ED. Undiagnosed liver abscess presented less abdominal pain and more symptoms or examination abnormalities related to infection of the respiratory and urinary tracts. Abdominal sonography should be performed more frequently at EDs to exclude liver abscess from differential diagnosis. However, further diagnosis and treatment while the patient with liver abscess is attending a ward does not affect prognosis.

Key Words: diagnosis, emergency department, liver abscess, prognostic factors
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Liver abscess may result in severe complications and even mortality. It often presents with nonspecific symptoms and diagnosis is often delayed. In some patients, liver abscess is not diagnosed in the

emergency department (ED) and is diagnosed later in the ward.

Diagnosis of liver abscess is based on computed tomography and sonography images [1,2]. However, before conducting such studies, the physician must suspect liver abscess based on the patient's symptoms or laboratory data. The classic symptoms and most laboratory examination abnormalities are nonspecific and indicate systemic infections. Abdominal pain and abnormal liver function tests are more specific but are not always present [3,4]. Delayed diagnosis and



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drainage of the liver abscess have been reported to be associated with poor prognosis [5,6]; however, the factors associated with the timing of diagnosis have not been reported.

Our aims were to identify the factors associated with diagnosis of liver abscess at an ED, and to determine whether liver abscess undiagnosed at an ED affects prognosis. Accordingly, we analyzed a series of patients with liver abscess, and compared them with patients in whom liver abscess was diagnosed or undiagnosed at an ED.

METHODS

We retrospectively collected patients who had been hospitalized in our hospital from 2005 to 2007 with a discharge diagnosis of liver abscess. All imaging and clinical data were reviewed. Patients were included if they had one or more echolucent lesions in the liver on ultrasonography or one or more hypodense area in the liver on computed tomography, plus at least one of the following: (1) collection of positive culture from either blood or percutaneous aspiration of the liver abscess; or (2) improvement and reduction in size of the imaging lesion after treatment for liver abscesses. The patients were all admitted to the ward from the ED ($n=177$). Tentative diagnoses at the ED were reviewed, and patients were classified into diagnosed or undiagnosed groups according to whether the tentative diagnosis included liver abscess.

Age, sex and underlying disease data were collected from medical records. Underlying diseases including hypertension, diabetes, malignancy, biliary tract disease and coronary artery disease were also recorded. Common symptoms of liver abscess and other respiratory and gastrointestinal symptoms were

collected from the ED. Common laboratory examinations and imaging findings used for infection survey were collected, including whole blood cell count, liver and renal functions, C-reactive protein levels, routine urine tests and chest X-rays. The serum glucose level was tested in some patients who were recorded as having diabetes associated with liver abscess. Time and type of antibiotic use in the ED were recorded. Diagnosis, location, amount and size of the liver abscess were all recorded, such as the time and procedure used for liver abscess drainage. Finally, the prognoses, including length of hospital stay, shock and mortality, were recorded.

Differences in variables between diagnosed and undiagnosed liver abscesses were analyzed. Continuous variables were analyzed by Student's *t* test and categorical variables were analyzed by χ^2 test or Fisher's exact test, as indicated. Statistical analyses were performed using SPSS version 13 (SPSS Inc., Chicago, IL, USA). A value of $p < 0.05$ was considered statistically significant.

RESULTS

There were 128 patients in the ED diagnosed group and 49 in the undiagnosed group, giving a diagnosis rate of 72.3%. The basic characteristics of the patients including age, sex and underlying disease are summarized in Table 1. There were no significant differences between the diagnosed and undiagnosed groups in terms of these factors.

Table 2 shows the common symptoms and usual examination results on presentation at the ED. Fever, chill and abdominal pain were the most common symptoms, and only abdominal pain showed a significant difference between the diagnosed and undiagnosed

Table 1. General characteristics of patients with liver abscess diagnosed or undiagnosed in the emergency department*

	ED diagnosed ($n=128$)	ED undiagnosed ($n=49$)	<i>p</i>
Age (yr)	61.5 ± 14.6	59.6 ± 17.1	0.454 [†]
Sex, male	64.1	71.4	0.354 [‡]
Diabetes mellitus	50.8	42.9	0.345 [‡]
Hypertension	39.8	30.6	0.256 [‡]
Coronary artery disease	5.5	0	0.192 [‡]
Biliary disease	37.5	22.4	0.057 [‡]
Malignancy	17.2	22.4	0.421 [‡]

*Data presented as mean ± standard deviation or %; [†]*t* test; [‡] χ^2 or Fisher's exact test. ED=Emergency department.

Table 2. Symptoms and signs of patients with liver abscess diagnosed or undiagnosed in the emergency department*

	ED diagnosed (n=128)	ED undiagnosed (n=49)	p
Fever	87.5	81.6	0.316 [†]
Symptom duration (d)	5.5±4.3	3.8±4.7	0.034 [‡]
Chills	65.6	53.1	0.123 [†]
Abdominal pain	73.4	42.9	<0.001 [†]
Nausea/vomiting	29.7	26.5	0.678 [†]
Respiratory tract symptoms	12.5	24.5	0.050 [†]
Consciousness disturbance	7.8	4.1	0.515 [†]
White blood cell count (/μL)	13,479±7,538	12,071±5,429	0.234 [‡]
>10,000/μL	71.9	63.3	0.266 [†]
Hemoglobin (g/dL)	12.2±2.2	12.3±2.4	0.794 [‡]
Anemia (males <13 g/dL, females <12 g/dL)	56.3	55.1	0.891 [†]
Platelet count (/μL)	205.5±134.6	185.7±96.1	0.349 [‡]
CRP (mg/L)	194.9±104.0	173.2±103.0	0.214 [‡]
>5 mg/L	99.2	95.9	0.186 [†]
>100 mg/L	82	73.5	0.205 [†]
AST (IU/L)	90.4±112.5	79.2±81.4	0.526 [‡]
>42 IU/L	61.7	61.2	0.952 [†]
>100 IU/L	25.8	16.3	0.182 [†]
ALT (IU/L)	85.0±92.6	76.6±101.3	0.602 [‡]
>40 IU/L	64.8	55.1	0.232 [†]
>100 IU/L	24.2	16.3	0.257 [†]
Glucose (mg/dL)	202.5±115.2	250.1±199.8	0.147 [‡]
Urea nitrogen (mg/dL)	18.5±10.5	20.2±12.7	0.378 [‡]
Creatinine (mg/dL)	1.25±0.77	1.36±0.98	0.422 [‡]
Pyuria	16.4	26.5	0.126 [†]
Pneumonia suspected on chest X-ray findings	4.7	14.7	0.048 [†]

*Data presented as mean±standard deviation or %; [†]χ² or Fisher's exact test; [‡]t test. ED=Emergency department; CRP=C-reactive protein; AST=aspartate aminotransferase; ALT=alanine aminotransferase.

groups (73.4% vs. 42.9%, *p*<0.001). Respiratory tract symptoms were reported by some patients with liver abscess, and were significantly less frequent in the diagnosed group than the undiagnosed group (12.5% vs. 24.5%, respectively, *p*=0.05).

Overall, 49 patients were admitted to wards without a confirmed diagnosis of liver abscess in the ED. Diagnosis was delayed by 1–14 days after presentation at the ED. The mean±standard deviation diagnosis delay was 4.41±3.16 days, with a median of 3 days. The tentative diagnoses at ED included fever, urinary tract infection and pneumonia (Table 3).

The mean diameter of liver abscess in the diagnosed and undiagnosed groups was 5.3±2.4 cm and

Table 3. Tentative diagnoses for patients with undiagnosed liver abscess in the emergency department (n=49)

Diagnosis	n
Fever	15
Urinary tract infection	14*
Pneumonia	10*
Biliary systems infection or disease	5 [†]
Diabetes complication	3 [‡]
Acute gastroenteritis	2
General weakness, hyponatremia	1

*One patient with pneumonia and urinary tract infection; [†]liver tumor, cholangitis, cholecystitis, biliary tract stone and complicated liver cyst; [‡]diabetic ketoacidosis, hyperglycemia, hyperosmolarity and poorly controlled diabetes mellitus.

Table 4. Prognosis of patients with diagnosed or undiagnosed liver abscess in the emergency department*

	ED diagnosed (n=128)	ED undiagnosed (n=49)	p
Length of hospital stay (d)	19.6±12.9	22.4±9.2	0.173 [†]
Shock	25 (19.5)	10 (20.4)	0.896 [‡]
In-hospital mortality	8 (6.3)	4 (8.2)	0.740 [‡]

*Data presented as mean±standard deviation or n (%); [†]t test; [‡]χ² or Fisher's exact test. ED=Emergency department.

4.8±2.5 cm, respectively. Overall, 49.2% and 36.7% of the liver abscesses in the two groups, respectively, was >5 cm. There was no significant difference in diameter ($p=0.204$) or percentage of large abscesses ($p=0.136$). Thirty (23.4%) patients in the diagnosed group had a liver abscess in the left lobe, 78 (60.9%) in the right lobe and 20 (15.6%) in both lobes. In the undiagnosed group, 10 (20.4%) patients had a liver abscess in the left lobe, 28 (57.1%) in the right lobe and 11 (22.4%) in both lobes. There were 86 (67.2%) patients with a single abscess in the diagnosed group and 29 (59.2%) in the undiagnosed group. There were no significant differences between the two groups in abscess location ($p=0.557$) or number of abscesses (single or multiple, $p=0.318$).

Shock was noted at the ED in 17 (13.3%) diagnosed patients and in three (6.1%) undiagnosed patients, but was not significantly different. Overall, 32 (25%) of the diagnosed patients underwent abscess drainage in the ED.

Antibiotics were given to most patients at the ED. The first dose was given within 3.29±2.27 hours in the diagnosed group and within 2.84±1.41 hours in the undiagnosed group. There was no difference between the two groups in terms of the time of starting antibiotic administration ($p=0.253$), but there was a difference in the types of antibiotics used between the two groups. Patients in the diagnosed group were given ampicillin/sulbactam (42/128, 32.8%), third-generation cephalosporin (41/128, 32.0%), first-generation cephalosporin (8/128, 6.3%), second-generation cephalosporin (7/128, 5.5%), amoxicillin/clavulanic acid (7/128, 5.5%) or no antibiotics (11/128, 8.6%). In the diagnosed group 44 (34.4%) patients were initially given metronidazole as combination therapy. The undiagnosed group was given first-generation cephalosporin (12/49, 24.5%), ampicillin/sulbactam (9/49, 18.4%), quinolones (5/49, 10.2%), second-generation cephalosporin (3/49, 6.1%), amoxicillin/clavulanic acid (3/49, 6.1%) or no antibiotics (11/49, 22.4%).

Pathogens were identified in 76.6% (98/128) of patients in the diagnosed group and in 69.4% (34/49) of patients in the undiagnosed group. The most common pathogens identified in culture-positive patients in the diagnosed and undiagnosed groups were *Klebsiella pneumoniae* (70.4% and 82.3%), and *Escherichia coli* (17.4% and 8.8%). There were three patients with amoebic infections (2 in the diagnosed group and 1 in the undiagnosed group). There were no significant differences between the two groups in terms of pathogen findings ($p=0.418$).

The mean length of hospital stay was 19.6±12.9 days in the diagnosed group versus 22.4±9.2 days in the undiagnosed group. Episodes of shock during hospitalization occurred in 25 (19.5%) and 10 (20.4%) patients in the diagnosed and undiagnosed groups, respectively. The rate of in-hospital mortality was 6.3% and 8.2% in the diagnosed and undiagnosed groups, respectively. There were no differences in these prognostic events between the two groups (Table 4).

DISCUSSION

Among the presenting symptoms for liver abscess, abdominal pain was more frequently reported in the diagnosed group while respiratory tract symptoms were more frequently reported in the undiagnosed group. Only abdominal pain increased the diagnosis rate of liver abscess, whereas symptoms in other sites may mask the diagnosis of liver abscess. However, no significant differences were found between the undiagnosed and diagnosed groups in terms of prognosis, including mortality, shock and length of hospital stay.

Previous studies have described the risk factors, symptoms and abnormal laboratory data for liver abscess. Being male, elderly, prior liver transplantation, and presence of biliary tract diseases, diabetes

or malignant tumor have been proposed as risk factors for liver abscess [3,7,8], but most of these underlying diseases may also be risk factors for other infectious diseases. Biliary tract diseases were more frequently noted in the diagnosed group, although this was not statistically significant. However, the presence of such risk factors, apart from biliary tract disease, does not aid the diagnosis of liver abscess. Common symptoms of liver abscess include fever, chills and abdominal pain [9]. Some patients may have malaise, anorexia, nausea and disturbed consciousness. Only abdominal pain was more specific for intra-abdominal infection, but the rate was low, ranging from 35% to 57% in previous studies [4,9]. The rate of abdominal pain in the present study was 65% and a significant difference was noted between the diagnosed and undiagnosed groups (42.9% vs. 73.4%, respectively, $p < 0.001$). Because the pain may not be severe and peritoneal signs are not always found during physical examination, physicians at the ED may not consider abdominal pain to be related to the infection. However, it is reasonable for an physicians at the ED to consider intra-abdominal infection if abdominal pain is present.

Laboratory findings are also nonspecific. The most sensitive items were C-reactive protein and serum albumin levels. Abnormalities in liver function tests were found in some patients (elevated aspartate aminotransferase, 61.6%; elevated alanine aminotransferase, 62.1%) but the abnormalities were usually mild (aspartate aminotransferase < 100 IU/L, 76.8%; alanine aminotransferase < 100 IU/L, 78.0%). Although abnormal liver function tests may indicate liver problems, they may be due to the presence of other systemic infections or underlying liver problems.

In our study, there were no significant differences in liver function tests between the two groups. This suggests that the abnormality did not prompt the physicians at the ED to consider liver infection. Of interest, more patients in the diagnosed group underwent liver abscess drainage while in the ED and more frequently received third-generation cephalosporin and ampicillin/sulbactam. Although the management of liver abscess differed in the ED between the diagnosed and undiagnosed groups, rates of mortality and shock, and length of hospital stay were not significantly different between the two groups. This may be explained because most of the undiagnosed patients in whom the liver abscess was found in the ward several

days after admission, received timely empiric antibiotics while they were in the ED.

In the 49 undiagnosed patients, the tentative diagnoses at the ED included fever, urinary tract infection and pneumonia. This occurred because physicians at the ED sometimes admit patients with a definitive diagnosis of fever for further examination in a ward setting, having not performed abdominal imaging in the ED. As shown in this study, liver abscess did not present with specific symptoms or abnormal laboratory data indicating intra-abdominal infection. Although physicians at the ED may not conduct abdominal imaging at the ED, liver abscess should be considered in the differential diagnosis of patients with fever exhibiting nonspecific symptoms and signs. Thus abdominal imaging should be considered at the ED. Coincidental respiratory tract infection symptoms, abnormal chest X-ray findings and pyuria would likely direct physicians to other tentative diagnoses for febrile patients. Few patients in our study, who were admitted to a ward under the impression of diabetes complications and hyponatremia, appeared to experience a long delay until diagnosis (10 days in a patient with diabetic ketoacidosis, 12 days in a patient with hyperglycemia and hyperosmolarity, and 14 days in a patient with hyponatremia). Thus uncommon presentations and other co-morbidities may affect the rate of diagnoses at the ED and in the ward.

Regarding the nonspecific finding of liver abscess, median duration of symptoms before admission was 14 days in the study by Mohsen et al [10]. In contrast, the duration of symptoms before admission was only 5.1 ± 4.4 days in our study. Most studies [4,8,11–15] have described that the underlying diseases and shock (severe clinical manifestation) are prognostic factors. Some studies [15–17] have also revealed that diabetes and being elderly are associated with the prognosis of liver abscess. The characteristics of liver abscess including gas formation or multiple factors were reported to be associated with poor prognosis in some studies [18,19]. Delayed diagnosis [6] and delayed drainage [5] are also associated with poor prognosis. No significant difference was noted between the diagnosed and undiagnosed groups in our study, although a delay to diagnosis was inevitable in the undiagnosed group. Because most patients were admitted to the ward for infection survey, abdominal sonography or other imaging studies were usually performed within a few days of admission to the ward. The mean

diagnosis delay was 4.41 ± 3.16 days, although delaying the diagnosis by a few more days is unlikely to markedly affect the prognosis.

In conclusion, except for abdominal pain, liver abscess usually presents with nonspecific symptoms and laboratory findings. Even abdominal pain is reported in only 65% of patients, for patients with fever, but without a definite diagnosis, liver abscess should be considered in the differential diagnosis. Abdominal imaging should be considered while the patient is at the ED to prevent unwanted delays in reaching a diagnosis; this is despite the fact that diagnosis after admission to a ward does not seem to significantly affect prognosis.

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急診未診斷之肝膿瘍病患臨床特徵

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肝膿瘍常以非特異性的症狀及血液檢驗異常做表現，使得病患可能無法在急診就能得到正確診斷。這項研究目的在比較能在急診診斷出的肝膿瘍病患，其在臨床表現上、檢驗數據上是否有所差異，而在急診診斷與否，是否會影響預後。研究回溯性收集2005–2007年診斷有肝膿瘍由醫院住院後出院的病患，將由急診入院的病患分為在急診已診斷出肝膿瘍以及之後在病房才診斷出肝膿瘍的病患，比較兩組病患的臨床表現、檢驗數據及各項預後。結果發現臨床表現有腹痛的病患（73.4% vs. 42.9%； $p < 0.0005$ ）及就診前症狀較久的病患（5.5天 vs. 3.8天； $p = 0.034$ ），和在急診診斷出肝膿瘍有相關，而呼吸道感染症狀（12.5% vs. 24.5%； $p = 0.05$ ）及胸部X光異常（4.7% vs. 14.7%； $p = 0.048$ ）和在急診診斷出肝膿瘍有負相關。在急診未診斷出肝膿瘍會讓診斷時間延後 4.41 ± 3.16 天。兩組病患在死亡率（6.3% vs. 8.2%； $p = 0.740$ ）、休克（19.5% vs. 20.4%； $p = 0.896$ ）及住院日數（19.6天 vs. 22.4天； $p = 0.173$ ）並無顯著差異。所以大多數在急診得到的病史、症狀及血液檢驗結果並不能幫助診斷，只有腹痛和急診診斷有高度相關，急診未診斷的肝膿瘍病患較無腹痛的表現，並較常同時有呼吸道或泌尿道的感染症狀或檢驗異常，對發燒不明病思考慮在急診進行腹部超音波檢查可增加肝膿瘍診斷，但進一步在住院後才診斷出肝膿瘍並不會明顯影響死亡率及住院日數等預後。

關鍵詞：診斷，急診，肝膿瘍，預後因子
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