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Pyogenic Liver Abscess and the Emergence of Klebsiella as an Etiology: a Retrospective Study

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ABSTRACT

Pyogenic liver abscess (PLA) is a significant, though uncommon, cause of morbidity in the United States. Recently, Klebsiella has emerged as an important cause of PLA. We analyzed the clinical course, microbiology, and treatment outcomes of patients discharged with PLA. In addition, we sought to examine the incidence of and risk factors for Klebsiella liver abscess (KLA). We identified 49 cases of PLA. Abscess cultures were positive in 23 (48%) patients. The mean age of the pts was 56 years (range: 20-83 years). Sixty percent were male. The most frequent conditions associated with PLA were intra-abdominal infections (ten cases; 20%), diabetes mellitus (nine cases; 18%) and malignancy (nine cases; 18%). Klebsiella was the most commonly isolated species from the abscess cultures (seven cases; 30% of all positive abscess cultures). We used univariate and logistic regression analyses to identify the risk factors for KLA. Controlling for age, only malignancy was identified in our study as a risk factor for a Klebsiella liver abscess. Klebsiella is emerging as an important cause of liver abscesses. Malignancy may be an important risk factor for Klebsiella liver abscess.

KEYWORDS :

Introduction

Pyogenic liver abscess , a suppurative infection of the hepatic parenchyma, can develop as a complication of abdominal and biliary infections, or following hematogenous bacterial seeding of the liver. It is often polymicrobial, with Streptococci and Escherichia coli being the most commonly reported pathogens. Klebsiella spp. have emerged in recent years as important causes of monomicrobial liver abscesses. The full spectrum of Klebsiella liver abscesses , their pathogenesis, associated risk factors, and typical outcomes are still under investigation. This retrospective study was designed to analyze the clinical features and treatment outcomes of patients with PLA.

Methods

The medical records of patients admitted to our hospital between 1st September , 2013 and 1st September 2014 were reviewed for a diagnosis of PLA. Cases were included if a patient with PLA was diagnosed by aspirating purulent material from a liver lesion in the presence of symptoms and signs consistent with the condition, laboratory findings, and compatible imaging studies (computed tomography [CT], or ultrasonography).

Data collection

The cases of patients with PLA were reviewed and the following data were collected:

1. Demographics: age, sex and, race.

2. Comorbid conditions already reported to be associated with PLA: diabetes mellitus; malignancy; intra- abdominal infection; and hepatobiliary pathology.

3. The presence of other comorbid conditions: congestive heart failure; chronic kidney disease; and liver cirrhosis.

4. Presenting clinical features: fever; chills; abdominal pain; nausea; vomiting; diarrhea; acute respiratory failure; acute kidney injury; and septic shock.

5. Admission laboratory values including: white blood cell count; hemoglobin; platelet count; serum albumin; total bilirubin; ; alkaline phosphatase; prothrombin time; blood urea ; serum creatinine; liver lesion aspirate and blood culture results; and in bacterial susceptibility to antibiotics.

6. Radiological features of the abscess: size of the abscess; number and location of the abscesses, if present; whether abscesses are unilocular or multilocular; the presence of gas in the abscess cavity; rim enhancement by contrast material; and the presence of the "cluster sign."

7. Drainage method employed: needle aspiration; continuous drainage using a percutaneous pigtail catheter; or open surgical drainage.

8. Antimicrobial therapy and duration.

9. Outcome information: length of hospital stay, suppurative complications; and vital status at hospital discharge.

Statistical analysis

Continuous data were expressed as a mean with its associated standard deviation or range. Categorical data were expressed as the number of subjects with a specified condition, or a clinical variable and its corresponding percentage. Chi square, Student's t-test and Fisher's exact test were used when necessary. Logistic regression analysis was used to analyze the risk factors associated with KLA. A P-value<0.05 was considered statistically significant.

Results

Between september 1st , 2013 and 1st september, 2014, 49 patients were identified with PLA by the criteria listed in the Definitions section. Twenty-nine patients (60%) were male. The lowest age was 20 years and highest age was 83 years with mean age 56 years. The most frequently associated conditions encountered were intra-abdominal infections in ten patients (20%), diabetes mellitus in nine patients (18%), and malignancy in nine patients (18%). Diabetes mellitus was the only known risk factor for PLA in five patients. Seventeen patients (35%) had no obvious cause or risk factor for PLA and

were classified as having a cryptogenic liver abscess. The probable etiology of PLA in our study is illustrated in Table 1. Other associated comorbidities in the study included liver cirrhosis in three patients (6%), congestive heart failure in two patients (4%), and chronic kidney disease in one patient (2%). The clinical features and biochemical parameters are summarized in Tables 2 and and3,3, respectively. In all of the reviewed cases, PLA diagnosis was established within 3 days of hospital admission.

Table 1
Etiology of pyogenic liver abscess,

1. Hepato–pancreatico–biliary; total of 20 cases (42%).

a. Benign Cholecystitis; 4 cases
b. Cholelithiasis;4 cases
c. Liver cirrhosis; 3 cases
d. Pancreatic abscess; 1 case
e. Malignant Pancreatic cancer; 5 cases
f. Hepatocellular carcinoma; 1 case
g. Cholangiocarcinoma; 1case
h. Ampulla of Vater adenocarcinoma; 1case

2. Extra-hepato–pancreatico–biliary; total of 6 cases (13%)

a. Benign Appendicitis; 2 cases
b. Diverticulitis; 1case
c. Pelvic abscess; 1 case
d. Infected omentum; 1 case
e. Malignant Esophageal cancer; 1 case

3. Diabetes mellitus alone; 5 cases (10%)

4. Cryptogenic liver abscess; 17 cases (35%)

Table 2 Clinical features of 48 patients with pyogenic liver abscess
1. Fever 39 (81%)
2. Abdominal pain 35 (73%)
3. Chills 23 (48%)
4. Gastrointestinal symptoms (nausea, vomiting, diarrhea) 6 (31%)
5. Septic shock 3 (6%)
6. Respiratory failure1 (2%)

Table 3 Abnormal laboratory findings in pyogenic liver abscess patients:
1. Hypoalbuminemia 45/46 (98%)
2. Prolonged prothrombin time39/43 (91%)
3. Leukocytosis38/48 (79%)
4. Anemia36/48 (75%)
5. Elevated alkaline phosphatase32/46 (70%)
6. Elevated serum aspartate aminotransferase27/46 (59%)
7. Elevated serum alanine aminotransferase24/46 (52%)
8. Thrombocytosis16/48 (33%)
9. Elevated blood urea nitrogen13/48 (27%)
10. Elevated creatinine11/48 (23%)
11. Hyperbilirubinemia7/45 (16%)

Radiological feature
Ultrasonography was the most commonly used imaging modality for the diagnosis of PLA, as it was used in 47 patients. One patient was diagnosed only by CT scan .

The radiological features are listed below;

1. Number of abcess, (one or more)
2. Location (right lobe, left lobe or bilober),
3. Uniloculer or Biloculer,
4. Average size,
5. Rim enhasment,
6. Gas in cavity

Microbiology
Aerobic and anaerobic cultures of blood and abscesses were obtained from all patients. Abscess cultures were positive in 23 (48%) patients; ten (44%) were monomicrobial and 13 (56%) were polymicrobial (≥2 organisms isolated). Klebsiella spp. were the most commonly isolated bacteria (seven cases; 30%); Klebsiella pneumonia was found in five cases, and Klebsiella oxytoca in two cases. Viridans streptococci were the second most commonly isolated organisms, found in six (26%) of the positive culture cases. Collectively, anaerobes (Fusobacterium sp., Bacteroid fragilis, Clostridium sp., and Prevotella sp.) were isolated in ten cases (43%). Only five patients had confirmed bacteremia; three had concordant blood and abscess culture results, and two had bacteremia with negative cultures in the abscess.

The number of organisms isolated from all positive liver abscess cultures (n=23).

Among the 14 isolated Gram-negative bacteria, four were third-generation cephalosporin-resistant microbes, among which three were extended spectrum beta-lactamase-producing bacteria. The same three bacteria were fluoroquinolone-resistant; there were no carbapenem-resistant isolates.

Klebsiella liver abscess
The Klebsiella spp. isolated from the abscesses were resistant to ampicillin in all cases, but they were susceptible to all other tested antibiotics. All patients underwent successful percutaneous drainage. None of the patients had Klebsiella bacteremia or developed metastatic suppurative complications, although one patient had a positive blood culture for a viridans streptococcal species.

Treatment and outcomes
When percutaneous aspiration was felt to be appropriate, typically a 20-gauge, fine aspiration needle was used to drain the abscess cavity under radiological guidance. When continuous drainage was deemed necessary, a percutaneous pigtail catheter was inserted. A follow up ultrasonography of the liver was typically performed 1–2 weeks later, and every 2 weeks thereafter if the abscess did not resolve on the first follow-up scan. Removal of the percutaneous drain was decided based on the patient's clinical and laboratory response.

39 patients (81%) underwent abscess aspiration via needle aspiration only. 6 patients (13%) underwent percutaneous drainage with an indwelling pigtail catheter. The 3 remaining patients (6%) were treated medically with intravenous antibiotics alone. One patient underwent open surgical drainage following a failed percutaneous drainage attempt.

All patients were started on antibiotics prior to abscess drainage. The time interval between antibiotic administration and drainage was less than 72 hours in all cases. Beta-lactam antibiotics were the most commonly used class, including 19 patients on piperacillin/tazobactam, 14 on meropenem, and three on imipenem. Six patients (12.2%) received beta-lactam antibiotics alone; 33 patients (67.3%) were treated with beta-lactam antibiotics plus some combination of vancomycin, metronidazole, and/or the antifungal agent fluconazole.

Fifteen patients (30.6%) were discharged on the same intravenous antibiotic regimen initiated on admission, including seven out of the 23 patients with positive culture results. Beta-lactam antibiotics continued to be the most commonly used medications at discharge, with and,ampicillin sulbactum & amoxicillin clavulanate being prescribed in 23 out of 33 patients.

The average duration of percutaneous drainage was 22±20 days (range: 4–56 days). The mean length of hospital stay was 20±22 days (range: 1–82 days).

Discussion
In this retrospective study, the risk factors, microbiology, treatment, clinical course, and outcomes of 48 patients with PLA are reviewed and reported. In our series, we have been able to identify an underlying, predisposing disease process associated with the abscess formation in two-thirds of the cases including hepato–pancreatico–biliary system problems and cancer. Cancer was present in 29% of the patients with an identified problem, which supports recent reports suggesting that this is an emerging risk factor for PLA. Consistent with other studies, ultrasonography mostly used in the detection of liver

abscesses,because less time consuming ,can be done without preparation as well as cheaper than CT.

An important finding in our study is that the incidence of KLA (30% of all positive abscess cultures) was higher than expected, suggesting the possible emergence of Klebsiella spp. as an important cause of liver abscess in our hospital. Malignancy was very common in the group with KLA in our study, indicating that cancer may be an important risk factor.

A community-acquired Klebsiella pneumoniae primary invasive liver abscess syndrome has been recognised in Asia for more than 20 years, with almost 1000 reported presentations published by 2008; it has been reported less frequently in other regions. Of interest are an absence of prior hepatobiliary disease, an association with diabetes, and a risk of metastatic spread. Community-acquired KPLA has been associated with severe metastatic complications. The reasons for the changing epidemiology away from Escherichia coli as the leading cause of pyogenic liver abscess are unclear, although selective pressure for Klebsiella through widespread amoxicillin use, to which it is almost universally resistant, has been postulated. K. pneumoniae is frequently found as part of normal faecal flora, and spread to the liver is thought to occur from the intestines via the portal system.Ordinarily, any bacteria reaching the liver would then be phagocytosed and killed, and failure of this defence is presumed to lead to the formation of liver abscesses. Diabetes was present in about 50%–70% of patients in our reference study , presumably conferring susceptibility by impairing neutrophil-mediated defence,and this also appears to be a risk factor for metastatic complications

Overall, the mortality in our study is among the lowest reported. Our findings confirm that the percutaneous approach for liver abscess drainage is safe and effective when combined with appropriate antimicrobial therapy. It has been previously reported that the presence of malignancy is a poor prognostic factor in PLA patients. We speculate that the low mortality observed in our study reflects the increasing awareness of the disease, early detection, and prompt initiation of appropriate drainage, along with the use of antimicrobial therapy.

In conclusion, PLAs continue to be an important, though uncommon, cause of morbidity among hospitalized patients. Although our patient sample size is small, it suggests that malignancy may be an important risk factor for KLA specifically, and this requires further investigation. Clinicians should maintain PLA in their differential diagnosis of patients who present with the risk factors and clinical scenarios of fever, abdominal pain, and liver lesions, since prompt diagnosis, percutaneous drainage of the abscess, and administration of intravenous antibiotics can shorten hospital stays and save lives.

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