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ORIGINAL ARTICLE

Is there any difference in pyogenic liver abscess caused by *Streptococcus milleri* and *Klebsiella* spp?: Retrospective analysis over a 10-year period in a regional hospital

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Background/Purpose: To compare the clinical characteristics of patients with *Streptococcus milleri* (SM) and *Klebsiella* spp. associated pyogenic liver abscess (PLA).
Methods: A retrospective study of patients with PLA due to SM and *Klebsiella* spp. was conducted. Clinical characteristics, laboratory and radiological features, management and outcomes were analyzed.
Results: From 2000 to 2009 inclusive, 21 and 140 patients had SM and *Klebsiella* spp. associated monomicrobial infected PLA, respectively. A higher incidence of active malignancy occurred in the SM group (14.3% vs. 3.6%, $p < 0.03$). The common clinical features of the patients were fever, chill and right upper quadrant pain. A longer duration (6.3 vs. 4.4 day, $p = 0.04$) of symptoms and a higher incidence of hepatomegaly (14.3% vs. 2.9%, $p < 0.01$) occurred in the SM group. Common laboratory and imaging abnormalities included: anemia, leukocytosis, high erythrocyte sedimentation rate and C-reactive protein, hypoalbuminemia, elevated total bilirubin and alanine aminotransferase, right hepatic lobe involvement, hypoechoic in ultrasonograpghy, rim enhancement and septal lobulation in computed tomography. The biliary tract disorder was the most common cause of the disease in the two groups. Patients with *Klebsiella* spp. associated PLA tended to have more complications: bacteremia (61.6% vs. 31.6%, $p < 0.01$) septic shock (33.6% vs. 19%, $p = 0.11$), disseminated intravascular coagulation (20.7% vs. 4.8%, $p = 0.04$), metastatic infections (10.7% vs. 0%, $p = 0.06$), acute renal and respiratory failure (5% vs. 0%, $p = 0.14$). However, both were effectively managed by the

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combination of antibiotics and image-guided aspiration with/without drainage, and their mortality rates were comparable to each other. Those patients with metastatic infection might need a longer duration (6.07 vs. 5.32 week, $p = 0.144$) of antibiotic therapy, which was due to the longer mean duration (3.85 vs. 2.86, $p < 0.04$) of an intravenous counterpart.
Conclusion: SM associated PLA tends to have a distinct clinical syndrome as compared with that of *Klebsiella* spp. with regard to risk factors, clinical manifestations and complications. However, both can be effectively treated with a combination of antibiotics and image-guided aspiration with/without drainage.

Introduction

Pyogenic liver abscess (PLA) has been recognized since the time of Hippocrates. It is the most common type of visceral abscess. In a report of 540 cases of intraabdominal abscesses, PLA accounted for 48% of visceral abscesses.[1] This condition is a potentially life threatening condition, with a mortality rate ranging from 10—40%. Traditionally, bacterial pathogens commonly associated with PLA include flora of the gastrointestinal tract, such as Escherichia coli and other members of the Enterobacteriaceae family, Streptococcus milleri (SM), Enterococcus species and anaerobes. Multiple studies have revealed that Klebsiella spp. has been emerging as the most important cause of PLA in the Asian population, and it also plays an important role in the Western population, as it accounts for about 25% of all cases.[2] Recently, SM group organisms have received increasing attention as potential pathogens.[3—5] A prospective study by Moore-Gillon et al found SM to be the most common organism isolated from PLA, being found in 13/16 (81.3%) patients.[5] The name, *Streptococcus milleri*, honoring the oral microbiologist W.D. Miller, was first proposed by Guhof in 1956, to describe a gamma hemolytic streptococcus found in an oral cavity.[3]There are three species in the SM group: *S. intermedius*, *S. constellatus* and *S. anginosus*. They are components of the normal flora of the oropharynx, gastrointestinal tract and uro-genital tract. These species share a common denominator in the clinical setting with *Klebsiella* spp. i.e., a marked tendency to cause abscess formation. In the past, the recognition of these organisms was hampered because of taxonomic confusion and thus their clinical significance may have been underrated. Recently, Whiley and Beighton observed that there were three DNA homology groups that correspond to the type strains of *S. constellatus*, *S. intermedius* and *S. anginosus*.[4] Because of uniformity in classifying these organisms and appropriate microbiological culture, an increased incidence of SM group associated liver abscesses has been observed in several reviews.[5] However, there is still a lack of in-depth reports regarding SM group associated liver abscess. Identifying the distinct clinical features of the SM group and the Klebsiella spp group enables us to start appropriate empirical antibiotic therapy. Thus, the aim of this study is to review the characteristics of patients with SM and *Klebsiella* spp. associated PLA in the following areas: risk factors, clinical features, characteristic features of liver abscess, treatment and outcome.

Methods

The records of patients discharged from Tuen Mun hospital in Hong Kong with a diagnosis of PLA (International Classification of diseases code, 572.0) between January 2000 and December 2009 were reviewed. Cases were identified through searching the hospital database (Clinical Management System of Hospital Authority of Hong Kong). Underestimation of actual caseload is possible, as coding might have not included patients suffering the underlying disease. Case definition required patients to have one or more filling defects on liver imaging (either ultrasound (US) or computed tomography (CT) scan) together with positive blood/pus cultures of SM and *Klebsiella* spp. Those PLAs with mixed growth were excluded. The clinical records of these patients were retrospectively reviewed, to obtain the demographic characteristics, clinical features, laboratory, imaging findings, treatment methods and final outcomes.

Looking for underlying etiology

The PLA was considered secondary to biliary tract disease in patients with a clinical picture of cholecystitis or cholangitis or documented biliary ductal abnormality. It was attributed secondary to portal spread, when there was documented infection or pathology in the distribution of portal venous circulation. It was considered secondary to systemic hematogenous spread when a documented bacteremic episode with another source of infection was found before the onset of PLA. Cryptogenic abscess was defined when there was no obvious source of infection after appropriate investigations.

Management strategies

In general, a broad-spectrum antibiotic was given after the initial sepsis work-up. Imaging was performed in every case of suspected PLA and percutaneous needle aspiration of liver abscess was selected if the abscess was greater than 3 cm in diameter or there was a feature of on-going sepsis, despite antibiotic treatment. The procedure was usually performed using a 22 G Chiba needle under real-time US or CT guidance in the radiology department. The decision for continuous catheter drainage was determined by the attending radiologists and the drainage was done by an 8

French pigtail catheter. Surgical drainage was reserved for patients who failed to respond to antibiotics and percutaneous drainage, or those who had a surgical indication requiring open surgical management. Lastly, follow-up imaging was performed to confirm the resolution of the liver abscess.

Statistical analysis

The data were compiled and analyzed by use of the commercial Statistical Package for the Social Sciences (SPSS) for Window (version 17.0, SPSS Inc., Chicago, Illinois, USA). All continuous variables were expressed as mean ± standard deviation (SD). Categorical variables were reported as percent. The Student *t* test, Chi-square test, Fisher's exact test and Mann-Whitney U test were used when appropriate. A *p* value of ≦ .05 was considered statistically significant.

Results

From January 2000 to December 2009 inclusive, a total of 319 patients were diagnosed with PLA, in which 21 and 140 patients were caused by the SM group and *Klebsiella* spp. associated monomicrobial infection, respectively.

The demographic characteristics of these patients are shown in Table 1. Male dominance was found in patients with *Klebsiella* spp. infection. Major comorbidities of patients in the SM group and *Klebsiella* spp. group were similar and they included hypertension, ischemic heart disease, diabetes mellitus and stroke. Active malignancy was present in three (14.3%) patients (one patient each with newly detected cholangiocarcinoma and cancer of the gallbladder, and one with cholangiocarcinoma on palliative management) of the SM group and four (3.6%) patients (three patients with cholangiocarcinoma, one with cancer of the pancreas) of the *Klebsiella* spp. group, with a statistically significant difference (14.3% vs. 3.6%, $p < 0.03$) between the two groups.

The clinical features of PLA caused by the SM group and *Klebsiella* spp. are shown in Table 1. The duration of the symptoms prior to admission of the SM group was longer than that of *Klebsiella* spp. (6.3 vs. 4.4 days, $p = 0.04$). As shown in Table 1, the most common presenting features of patients of both groups were fever and chills, followed by right upper quadrant pain and diarrhea, with no statistically significant difference between the two groups, except that more patients in the SM group experienced abdominal pain (66.7% vs. 47.1%, $p < 0.05$). Jaundice was not a common feature in the two groups. Hepatomegly was more commonly seen in the SM group (14.3% vs. 3.9%, $p < 0.01$).

The laboratory findings are summarized in Table 2. Anemia, leukocytosis, high erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), hypoalbuminemia, elevated total bilirubin and alanine aminotransferase were the common features, while the patients with *Klebsiella* spp. associated PLA had a higher serum level of total bilirubin (34.6 vs. 18.6 μmol/L, $p < 0.05$) and alanine aminotransferase (106 vs. 57 U/L, $p < 0.02$). More patients with *Klebsiella* spp. associated PLA were bacteremic on admission (61.6% vs. 31.6%, $p < 0.01$).

US and CT of the abdomen were performed in 6 (28.6%) and 1 (4.8%) patients in the SM group, and 40 (28.6%) and 12 (8.6%) patients in the *Klebsiella* spp. group, respectively. Combined imaging was performed for 14 (66.7%) patients and 88 (62.9%) patients with SM and *Klebsiella* spp., respectively. The characteristics of PLA found in radiological imaging are shown in Table 2. More than 2/3 patients had a liver abscess at the right hepatic lobe and about 1/10 patients had bilobar involvement, with no statistically difference between the two groups. The mean size of the SM associated PLA was 0.9 cm larger than that of the *Klebsiella* spp. group, with no statistical difference. More

Table 1 Demographic and clinical characteristics of patients with SM and *Klebsiella* spp. group associated PLA

Variable	SM ($n = 21$)	*Klebsiella* spp. ($n = 140$)	*p*
Age, mean (SD)	59 (11.3)	64.8 (13.8)	0.164
Sex, male:female	10:11	79:61	—
Comorbidities			
Diabetic mellitus	4 (19%)	48 (34.3%)	0.08
Hypertension	4 (19%)	32 (22.9%)	0.34
Ischemic heart disease	1 (4.8%)	8 (5.7%)	0.44
Stroke	1 (4.8)	7 (5%)	0.49
Underlying active malignancy	3 (14.3%)	4 (3.6%)	<0.03
Duration of symptoms before presentation, mean days (SD)	6.3 (4.1)	4.4 (3.8)	**0.04**
Symptoms and signs			
Fever and chill	17 (85.7%)	132 (95%)	0.07
Right upper quadrant pain	14 (66.7%)	66 (47.1%)	**<0.05**
Diarrhea	2 (9.5%)	8 (5.7%)	0.25
Cough and sputum	3 (14.3%)	35 (25%)	0.14
Jaundice	1 (4.8%)	9 (6.4%)	0.39
Hepatomelgy	3 (14.3%)	4 (2.9%)	**<0.01**
Right pleural effusion/consolidation (on admission)	4 (19%)	18 (12.9%)	0.22

Data are no. (%) unless otherwise indicated. Boldface type indicates statistical significance.

Table 2 Laboratory findings and radiological features of patients with SM and *Klebsiella* spp. group associated PLA

Laboratory parameters	SM (n = 21)	*Klebsiella* spp. (n = 140)	p
Hemoglobulin (g/dL)	10.9 (1.9)	11.4 (1.8)	0.33
White cell count (10^9/L)	19.1 (5.1)	16.4 (3.3)	0.16
Erythrocyte sedimentation rate (mm/hr)	82.6 (11.1)	77.6 (17.7)	0.60
C-reactive protein (mg/L)	81.8 (27.2)	165 (36.2)	0.06
Albumin (g/L)	29.1 (6.3)	29.4 (4.9)	0.81
Total bilirubin (μmol/L)	18.6 (5.5)	34.6 (8.7)	**< 0.05**
Alanine aminotransferase (U/L)	57 (22.0)	106 (46.2)	**< 0.02**
Bacteremia[$]	6 (31.6%)	85 (61.6%)	**< 0.01**
Radiological features			
Size [cm, mean (SD)]	7.4 (2.9)	6.5 (2.8)	0.19
Site			
Right lobe	15 (71.4%)	97 (69.3%)	0.42
Left lobe	4 (19.1%)	31 (22.1%)	0.38
Bilobar	2 (9.5%)	12 (8.6%)	0.44
Echogenicity			
Hypoechoic	15 (71.4%)	95 (67.9%)	0.37
Hyperechoic/heterogenous	2 (9.5%)	12 (8.6%)	0.44
Thickened wall[$$]	7 (33.3%)	24 (17.1%)	**0.04**
Rim enhancement	12 (57.1%)	68 (48.6%)	0.23
Septal lobulation	13 (61.9%)	84 (60%)	0.43
Aerobila	0 (0%)	9 (6.4%)	0.12
Fluid/gaseous cavitation	19/2 (91%/9.5%)	124/13 (89%/9.3%)	0.39/0.49
Portal thrombophlebitis	1 (4.8%)	2 (1.4%)	0.13
Subcapsular rupture of the abscess	0 (0%)	6 (4.3%)	0.16

[$] Blood culture examination was not taken in two patients from each group on admission.
[$$] Defined as wall thickness > centimeter.[25]
Data are mean (standard deviation) or no. (%) of patients, unless otherwise indicated. Boldface type indicates statistical significance.

than 2/3 of the PLAs within the two groups appeared as hypoechoic nodules in US imaging; their common CT imaging features were rim enhancement, lobulated outline and central fluid/gas formation, with no statistically significant differences between the two groups. More abscesses in the SM group had a thickened wall, as compared with those in the other group (33.3% vs. 17.1%, $p = 0.04$), and no abscess rupture was found in the SM group (0% vs. 4.3%, $p = 0.16$).

The etiologies of the two groups are summarized in Table 3. Although > one-third of the cases had not been investigated for the underlying pathology, the biliary tract disorder was the most common cause of the disease in the two groups. One patient of the SM group had endoscopic retrograde cholangiopancreatography (ERCP) performed, and there was no abnormality detected, while 67 (47.9%) patients in the *Klebsiella* spp. group had ERCP and the findings included: 38 (56.7%) normal findings, eight (11.9%)

Table 3 The pathogenesis and confirmatory investigations of patients with SM and *Klebsiella* spp. group associated PLA

Pathogenesis	SM (n = 21)	*Klebsiella* spp. (n = 140)	p
Biliary tract disorder	8 (38.1%)	81 (57.9%)	0.05
Portal pyemia	0 (0%)	4 (2.9%)	0.20
Hematogenous	0 (0%)	3 (2.1%)	0.24
Cryptogenic	2 (9.5%)	9 (6.4%)	0.30
Not investigated	11(52.4%)	43 (30.7%)	**0.02**
Endoscopic retrograde cholangiopancreatography	1[a]	67[b]	
Endoscopic ultrasound	2[a]	6[c]	
Magnetic resonance cholangiopancreatography	2[a]	7[c]	
Colonoscopy	0	7[d]	

[a] All cases had normal findings.
[b] Common bile duct calculi(n = 8),benign ductal stricture (n = 6), malignant ductal stricture (n = 2), dilated common bile duct (n = 5), gallbladder stones (n = 6), failed (n = 2), normal (n = 38).
[c] One case had common bile duct stone while the others were normal.
[d] Colonic diverticulitis (n = 1), normal (n = 6).

common bile duct stones, six (9.0%) benign common bile duct stricture, two (3.0%) malignant bile duct stricture, five (7.5%) dilated common bile duct, six (9.0%) gallbladder stones, two (3.0%) failed procedure. Endoscopic ultrasound (EUS) and magnetic resonance cholangiopancreatography (MRCP) were introduced into our department in 2008 and 2007. From 2008, EUS was performed in two and six patients (aged 42−71 years, median age = 55 years) from the SM and *Klebsiella* spp. groups, respectively; common bile duct stone was found in one patient of the *Klebsiella* spp. group while the others had normal findings. MRCP was performed in two and seven patients of the SM and *Klebsiella* spp. groups, respectively; a common bile duct stone was seen in one patient of the *Klebsiella* spp. group, while the others had normal findings. Colonoscopy was performed in seven patients of the *Klebsiella* spp. group since 2007 and only one patient had features of colonic diverticulitis while the others had normal findings.

The management and outcomes of the two groups are summarized in Table 4. All patients received intravenous broad-spectrum antibiotics after assessment for sepsis. Extended-spectrum penicillin (36.6%), third (32.9%) and second (21.1%) generation cephalosporins were the commonly used intravenous antibiotics, in which the third-generation cephalosporin was used more in the *Klebsiella* spp. as compared with that in the SM group (35.7% vs. 14.3%, $p < 0.03$) and the latter group tended to use extended-spectrum penicillin more (52.4% vs. 34.3%, $p = 0.054$). The commonly used oral antibiotics were: extended-spectrum penicillin, quinolones and oral second generation cephalosporins, in which more than 2/3 of patients with the SM group associated PLA were treated with penicillin (76.2% vs. 36.4%, $p < 0.01$) and about 1/5 of patients in the *Klebsiella* spp. group had taken oral quinolones (22.9% vs. 0%, $p < 0.01$). Although there was no statistically significant difference in the mean duration of antibiotic treatment between the two groups (5.3 vs. 5.4 week, $p = 0.47$), the SM group tended to have a shorter duration (2.2 vs. 3.1 weeks, $p < 0.03$) of intravenous portion and a longer duration (3.2 vs. 2.3 weeks, $p = 0.04$) of oral portion of the antibiotic as compared with those of Klebsiella spp group. Isolates from PLAs of the SM group had no antibiotic resistant strains, whereas eleven (7.9%) isolates from the *Klebsiella* spp. group had resistant strains (0 vs. 7.9%, $p = 0.09$). There were no isolates with extended spectrum β-lactamase (ESBL) in our study. The time to appropriate antibiotic was instant in the SM group; there was a 0.39 ± 0.02 (mean ± SD) day delay in having an appropriate antibiotic prescription in the *Klebsiella* spp. group, without any statistically significant difference. The antibiotic therapy was the only treatment for two (9.5%) and seven (5%) patients of the SM and *Klebsiella* spp. groups, respectively, and the reason for not performing image-guided aspiration and drainage was the small size of the lesion (<3 cm in diameter). The mean time intervals to having imaging-guided intervention were 3.6 and 2.8 days in the SM and *Klebsiella* spp. groups, respectively, without statistical significant difference. Among the SM group, US-guided needle aspiration was performed in 18 (86%) patients and continuous catheter drainage was performed

Table 4 The management and outcomes of the patients with SM and *Klebsiella* spp. group associated PLA

	Management		
Antibiotic	SM ($n = 21$)	*Klebsiella* spp. ($n = 140$)	p
Time to appropriate antibiotic [day, mean (SD)]	0 (0)	0.39 (0.02)	0.46
Intravenous, week, mean (SD)	2.2 (1)	3.1 (1.7)	**<0.03**
Extended-spectrum penicillin	11 (52.4%)	48 (34.3%)	0.054
Second generation cephalosporin	4 (19%)	30 (21.4%)	0.4
Third generation cephalosporin	3 (14.3%)	50 (35.7%)	**<0.03**
Oral, week, mean (SD)	3.2 (2)	2.3 (1.6)	**0.04**
Extended-spectrum penicillin	16 (76.2%)	51 (36.4%)	**<0.01**
Second generation cephalosporin	3 (14.3%)	27 (19.3%)	0.29
Quinolone	0 (0%)	32 (22.9%)	**<0.01**
Intervention			
Time interval to have intervention [day, mean(SD)]	3.6 (1.4)	2.8 (1.1)	0.48
Imaging-guided aspiration ± drainage	18/15 (86%/71%)	125/109 (89%/78%)	0.34/0.4
Surgical drainage	1 (4.8%)	8 (5.7%)	0.43
Complications and Outcomes			
Metastatic infection	0 (0%)	15 (10.7%)	0.06
Septic shock	4 (19%)	47 (33.6%)	0.11
DIC[#]	1 (4.8%)	29 (20.7%)	**0.04**
Acute coronary syndrome	0 (0%)	8 (5.7%)	0.13
Respiratory/renal failure	0 (0%)	7 (5%)	0.14
ICU care[$]	2 (9.5%)	16 (11.4%)	0.40
Death	3 (14.3%)	12 (8.6%)	0.20

[#] For disseminated intravascular coagulation.
[$] For intensive care unit.
Data are no. (%) of patients, unless otherwise indicated. Boldface type indicates statistical significance.

in 15 (71.4%) patients; in the *Klebsiella* spp. group, 125 (89.3%) patients had US-guided needle aspiration and among these, 109 (77.9%) patients had continuous catheter drainage. A pigtail catheter was not inserted in these 19 patients after percutaneous aspiration, because the abscess was too solid or it was completely collapsed after aspiration and thus, further catheter drainage was considered not useful. Surgical drainage was required in 1(4.8%) and 8 (5.7%) patients in the SM and *Klebsiella* spp. groups, respectively; the main indication of laparotomy among these patients was the presentation of acute abdomen. No patients failed to respond to antibiotics, with/without percutaneous drainage.

Patients in the *Klebsiella* spp. group tended to have more adverse events than did patients in the SM group, as there were more instances of bacteremia (61.6% vs. 31.6%, $p < 0.01$), septic shock (33.6% vs. 19%, $p = 0.09$), disseminated intravascular coagulation (DIC, 20.7% vs. 4.8%, $p = 0.04$), acute renal and respiratory failure (5% vs. 0%, $p = 0.14$) in patients of *Klebsiella* spp. group. The distant spread of the infection was detected in 15(10.7%) patients (seven patients with urinary tract infection, three with endophthalmitis, two with pneumonia, one each with right empyema, right psoas abscess and simultaneous endophthalmitis and urinary tract infection) of the *Klebsiella* spp. group, whereas all patients of the SM group had a localized septic process without distant spread (10.7% vs. 0%, $p = 0.06$). The PLAs with distant spread tended to have a longer duration of antibiotics than those PLAs without (6.07 vs. 5.32 weeks, $p = 0.144$; data not shown); this was due to the longer mean duration of intravenous antibiotics (3.85 vs. 2.86, $p < 0.04$; data not shown). The mortality rates of both groups were comparable to each other. There were 3(14.3%) deaths in the SM group and all were cancer-related; two patients (one of them was newly diagnosed) with cholangiocarcinoma and one patient with cancer of the gallbladder. The *Klebsiella* spp. group had 12 (8.6%) deaths; three cholangiocarcinoma, two cerebrovascular accident, two respiratory failure, one each of cancer of the pancreas, uncontrolled bleeding duodenal ulcer and congestive heart failure.

Discussion

PLA is the most common type of visceral abscess with significant morbidity and mortality. The incidence is expected to increase with the risk factors including age, diabetic mellitus and malignancy. Over the past few decades, there have been observed significant changes in etiology, bacteriology, diagnosis and management of PLA.[6–8] Recent reports reveal two important trends in the pathology of PLA: *Klebsiella* spp. becomes one of the most common organisms identified in Asian and Western populations, and *S. milleri* is recognized as an emerging pathogen with a catch-up increase in incidence.

In this study, the mean age of the SM group was lower than that of the *Klebsiella* spp. Group; by contrast, the duration of symptoms prior to admission was longer in the SM group. These were related to a higher proportion of patients with *Klebsiella* infection caused by a biliary tract disorder which is more commonly seen in elderly patients. Seeto and Rockey found that PLA presented most acutely (3 days) if it was due to bilary tract disorder.[9] There was male dominance in both groups, as in most previous reports.[10–16] Diabetic mellitus was more associated with the *Klebsiella* spp. group, but the figure was not as high as those of previous Taiwan studies.[11] The predilection for PLA in diabetic mellitus remains unclear, but the possible mechanism is the impairment of phagocytosis of the pathogen.[17] It is a well-known fact that the underlying active malignancy is also a risk factor and in this study, the association was stronger with the SM group. The reason may be that SM, a facultative anaerobe, grows more favorably in tumors that are more acidic and hypoxic than in normal tissue.

The clinical manifestations of the patients of both groups in the present study were similar to each other; fever, chills and right upper quadrant pain were frequent symptoms. However, the patients in the SM group were more likely to experience right upper quadrant pain and hepatomegaly, which may be explained by a higher incidence of intrahepatic malignancies in this group. One-fifth of both groups had an abnormality detected in the chest radiograph, without any localizing signs in the abdomen, which might cause a misdiagnosis of pneumonia. Laboratory abnormalities were similar between the two groups, mainly anemia, leukocytosis, high ESR and CRP, and deranged liver function with elevated serum bilirubin and alkaline phosphatase. The changes in bilirubin and alkaline phosphatase were more pronounced in the *Klebsiella* spp. group, which may be due to its higher incidence of biliary tract disorder. The predominance of right-lobe involvement was found in both groups, which is consistent with prior reports. The right lobe was most commonly involved due to its size and propensity to receive most of the portal blood flow. The US and CT appearance of both groups were similar to each other. The former may range from hyperechoic to hypoechoic and this variation has a close relationship to the pathologic stage of PLA. During the very early stage of abscess formation, the hepatocytes undergo acute inflammation and thus the abscess might appear solid, i.e. hyperechoic. When the hepatocytes start necrosis, the abscess becomes liquefied with increasing fluid content and surrounding edema. This is also the stage at which most patients with PLA present clinically; thus most PLA are hypoechoic at US and are fluid-containing lesions with rim enhancement in CT contrast study, which are consistent to our findings. Gaseous cavitation was an infrequent feature in this study, which is in agreement with previous studies.[10,12,15] In this study, a higher incidence of abscess rupture in the *Klebsiella* spp. group might be accounted for by its wall thickness and size.

As in recent reports, biliary disease was the most common identifiable cause of PLA in our patients. Although Chua et al found that 1/4 patients with SM group associated PLA were caused by Crohn's disease,[18] our results did not support this finding. This is because inflammatory bowel disease in populations in Asian regions is still not as common as that in Caucasians.[19] Searching for an underlying cause is not routinely performed in our institution, but in past few years, noninvasive imaging techniques, like EUS and MRCP, have been increasingly used to define the biliary anatomy instead of ERCP. A substantial number of our cases were considered cryptogenic in both groups,

although colonoscopy, ERCP and EUS were performed in poor coverage.

In our study, both groups of PLA were well managed by a combination of antibiotics and imaging-guided aspiration with/without drainage. The empirical antibiotic should cover both spectra of Gram positive cocci and Gram negative bacilli. Although antibiotic resistance was not common in both groups, one should be alert to this possibility if the clinical condition of the patient does not respond to the treatment. In our study, all isolates of the SM group were sensitive to an extended-spectrum of penicillin and this might be due to the incidence of SM related PLA not as high as that of *Klebsiella* spp. related. We expect SM resistant strains will appear with an increasing incidence of SM related PLA, similar to the situation in *Klebsiella* spp. infection. Our findings showed that 10% of Klebsiella isolates were resistant to penicillin, but all were sensitive to quinolones and third generation cephalosporins. Nevertheless, one should be alert to the possibility of the development of increasing antibiotic resistant strains in the future. Patients in the *Klebsiella* spp. group received appropriate antibiotic treatment with a small non-statistical delay, as compared to those of the SM group, owing to the presence of the resistant strain. We expect this figure may increase with the incidence of antibiotic resistance and subsequently this, together with the associated adverse events, may have clinical implications. The duration of antibiotic treatment in PLA has been based on clinical experience of the clinician. Gao et al reported that C-reactive protein can be used as a guide to determine the duration of antibiotic treatment for PLA after complete percutaneous drainage.[20] The implication of a shorter intravenous and longer oral antibiotic duration in the SM group, as compared to the *Klebsiella* spp. group, is the ability to switch over early to the oral counterpart once the clinical condition, such as body temperature, white cell count and CRP level, of the patient is in remission. This has a good economic impact of shortening the length of stay in hospital. The higher incidence of bacteremia, septic shock, DIC, organ failure and acute coronary syndrome in the *Klebsiella* spp. group indicates the need for suspicion of PLA if blood culture yields *Klebsiella* spp.; abdominal imaging and appropriate antibiotics should be initiated without any delay.

The previous study reported that the metastatic infection rate of *Klebsiella* spp. group was higher than *non-Klebsiella* group and that the endogenous endophthalmitis was the predominant site of involvement.[21] Our data showed that this clinical feature did not confer any delay in appropriate antibiotic and imaging-guided intervention. Yang et al found that the K1 capsular serotype of *Klebsiella* spp. associated with metastatic infection, owing to its production of mucoviscous exopolysaccharide webs that are resistant to complement-mediated serum killing and thus allows bacilli to spread.[22] Of these patients, 75% were diabetic. The hypothesis of diabetic association is that intimal vascular defect in diabetic patients may predispose to hematogenous seeding of *Klebsiella* spp., and cause liver abscesses and metastatic infections.[23] In this study, the incidence of metastatic infections in the *Klebsiella* spp. group was markedly higher than in the SM group; these infections were associated with a longer duration of antibiotics, particularly the intravenous counterpart. This implies that patients complicated with metastatic infection, may require a longer time to achieve clinical remission. In contrary to the previous Tawian studies, our results showed that the most common site involved was the urinary tract (8/15, 53.3%); the endogenous endophthalmitis was the second most prevalent (4/15, 26.7%). Half of the patients with metastatic infection were diabetic. All of the urinary tract infections were asymptomatic and most of the patients with endogenous endophthalmitis presented with subacute vision impairment. The incidence of metastatic infection might be under-estimated. Therefore, a high index of clinical suspicion and the close monitoring of those confirmed cases are warranted.

In this study, the mortality rate of SM and Klebsiella spp associated liver abscesses were 14.3% and 8.6%, respectively, which are comparable with other studies.[24] No general consensus has been achieved regarding prognostic factors, and this may be due to differences in subject populations.

In conclusion, the *Streptococcus milleri* associated pyogenic liver abscess tends to have a distinct clinical syndrome as compared with that of *Klebsiella* spp., in regard to the different extent of risk factors, including a small increase in risk of abdominal malignancy, clinical manifestations and complications. However, both can be effectively managed by the combination of antibiotic and image-guided aspiration with/without drainage and their mortality rates are comparable each other. Those with metastatic infection might require a longer duration of antibiotics, particular the intravenous counterpart.

Authors' contributions

STL and KKL were responsible for the patient care.

STL was also responsible for the conception and writing of the manuscript. All authors read and approved the final manuscript.

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Conflicts of interest statement

The authors declare that they have no conflicts of interest.

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