

Characteristics of Pyogenic Liver Abscess

Experience of a single centre in Oman

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ABSTRACT: Objectives: This study aimed to analyse the epidemiological, aetiological and clinical characteristics of pyogenic liver abscess (PLA) occurring in Oman. The intention was to obtain the information needed for the adequate liver abscess (LA) empirical treatment. LA can develop as a complication of hepatobiliary disease or other intraabdominal infections, but more recently, it is associated with primary and secondary liver malignancies and their treatment. **Methods:** This retrospective study took place in the Royal Hospital, Muscat, Oman. Consecutive patients treated for LA from January 2013 to December 2017 were enrolled. Their demographic and clinical data were used to study the characteristics of PLA occurring in Oman. **Results:** A total of 53 patients with PLA were enrolled in the study. They were predominantly male and younger than 60 years. *Klebsiella pneumoniae* was found to be the most common bacteria causing LA. Clinical presentation was non-specific, and abdominal pain and high fever were the most common symptoms. **Conclusion:** The majority of PLAs are caused by *K. pneumoniae*, so the empirical treatment should begin with antibiotic directed against it. Further studies are needed to establish the local role of anaerobic bacteria in PLA and monitor the presence of hypervirulent *K. pneumoniae* in Oman.

Keywords: Pyogenic Liver Abscess; Etiology; Epidemiology; *Klebsiella pneumoniae*; Oman.

ADVANCES IN KNOWLEDGE

- This study is the first to analyse the clinical, epidemiological and aetiological aspects of pyogenic liver abscess (PLA) occurring in Oman.
- *Klebsiella pneumoniae* is the most common cause of PLA in Oman.
- The majority of patients have the cryptogenic form of liver abscess.

APPLICATION TO PATIENT CARE

- Identifying the PLA characteristics in the Omani population will help the healthcare practitioners to plan the appropriate differential diagnosis workup and start the adequate empirical treatment.

LIVER ABSCESS (LA) IS DEFINED AS AN ENCAPSULATED collection of pus within the liver parenchyma. LAs are predominantly caused by bacteria generating a pyogenic liver abscess (PLA), while parasites and fungi are less common LA causes.¹ During the early years of the 20th century, PLA was seen mostly as secondary to appendicitis, but later, biliary tract diseases usually preceded PLA.² More recently, PLAs can occur because of secondary infection of a primary liver tumour or metastatic liver lesions as well as their treatments, particularly as complications of trans-arterial chemoembolisation or radiofrequency ablation.^{3,4} In the situation where no obvious source of extra-hepatic infection is determined following a full investigation, PLA is labelled as cryptogenic.⁵

The prevalence of cryptogenic PLAs varies throughout the world. It reached 17% in the UK and France, while in Australia and Asia, it was 34% and 65%, respectively.⁶ Previous studies showed a significant difference in PLA aetiology. In Europe and North America, *Escherichia coli*, *Staphylococcus* spp., *Streptococcus* spp. and *Enterococcus* spp. are

the most common causes of PLA, while in Asia, the predominant cause is *Klebsiella pneumoniae*.⁷ Moreover, several studies showed that *K. pneumoniae* is the main cause of cryptogenic PLA regardless of geographical distribution.^{6,8} However, the characteristics of PLA in Gulf countries are not well known. To the best of the authors' knowledge, only one study from Qatar and a few case reports from Oman and Saudi Arabia that describe PLA have been published till date.^{9–11} This retrospective study aimed to establish the epidemiological, aetiological and clinical characteristics of PLA in Oman.

Methods

The study was conducted at the Royal Hospital, Muscat, Oman, by collecting patients' data from the Royal Hospital database. All patients >13 years old who were treated for LA during the five-year period from January 2013 to December 2017 were enrolled in the study. The LA aetiology was determined by abscess and/or blood culture. The blood for the aerobic and

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anaerobic culture was taken at admission, and if the patient underwent the abscess percutaneous drainage procedure, the pus sample was sent for the aerobic culture. Amoebic abscess was diagnosed using a commercial immunoglobulin G (IgG) anti-amoebic assay (R-Biopharm AG, Darmstadt, Germany). Patients with confirmed amoebic LA were excluded. To trace a possible but undetected underlying PLA source during hospitalisation, after the discharge, the patients were followed-up through the hospital database system for one to six years.

The approval for the study was obtained from the Royal Hospital Scientific Research Committee (SRC#32/2018).

Results

During the five-year study period, 76 patients were treated for LA. Of these, 53 had PLA, while the remaining had amoebic LA and, thus, were excluded from the analysis. Out of the 53 selected, 40 (75.5%) patients were male and 13 (24.5%) were female. The mean age of the whole group was 46.8 years (range: 14–92 years). When comparing the average age of male and female patients, no statistical difference was observed, although the mean ages for the male and female patients were 51.3 and 44.7 years, respectively. The clinical presentation of PLA was non-specific and upper abdominal pain was the most common symptom, being found in 42 (79.3%) patients. Fever was present in 31 patients (58.5%) and 13 (24.5%) were observed to be icteric. At the time of admission to the hospital, 34 (64.2%) patients had leukocytosis above $10 \times 10^9/L$ (reference range: $2.4-9.5 \times 10^9/L$). Alanine aminotransferase (ALT) above 40 IU/L (reference range: 0–40 IU/L) was found in 30 (56.6%) patients and bilirubin above 20 mmol/L (reference range: 0–20 mmol/L) in 18 (34.0%) patients.

The definite PLA diagnosis was established by a computed tomography (CAT) scan, magnetic resonance imaging or abdominal ultrasound. A total of 35 (66.0%) patients had a single abscess. In 33 (62.3%) patients, PLA was found in the right liver lobe. In 13 (24.5%) patients, it was in the left lobe, while in seven (13.2%) patients, both lobes were involved. The average PLA size was 6.3 cm with median of 6 cm and the size ranged from 2 to 14 cm. The majority of the patients ($n = 34$; 64.2%) had cryptogenic PLA [Table 1].

Of the 53 patients, blood and/or abscess culture were positive in 30 (62.3%) patients, while in the rest, PLA aetiology was not determined since the cultures remained sterile. *K. pneumoniae* was the most common bacteria causing PLA, and it was found in 22 patients,

Table 1: Characteristics of patients with pyogenic liver abscess treated at the Royal Hospital, Muscat, Oman, between January 2013 and December 2017 (N = 53)

Characteristic	n (%)
Gender	
Female	13 (24.5)
Male	40 (75.5)
Age in years	
<60	36 (67.9)
>60	17 (32.1)
Symptoms	
Fever	31 (58.5)
Abdominal pain	42 (79.3)
Jaundice	13 (24.5)
Laboratory results	
WBC >10	34 (64.2)
ALT >40	29 (54.7)
Comorbidity	
Hepatobiliary disease	17 (32.1)
Immunosuppression	3 (5.7)
Intraabdominal trauma	1 (1.9)
Diabetes mellitus	15 (28.3)
None	12 (22.6)

WBC = white blood cells; ALT = alanine transaminase.

Table 2: Aetiology of pyogenic liver abscess of patients treated at the Royal Hospital, Muscat, Oman, between January 2013 and December 2017 (N = 53)

Aetiology	n (%)	
	Blood culture (n = 48)	Abscess culture (n = 37)
<i>Klebsiella pneumoniae</i>	5 (10.4)	17 (46.0)
<i>Escherichia coli</i>	1 (2.1)	3 (8.1)
<i>Enterococcus</i> spp.	1 (2.1)	1 (2.7)
<i>Pseudomonas aeruginosa</i>	0 (0)	1 (2.7)
<i>Staphylococcus aureus</i>	0 (0)	1 (2.7)
<i>Streptococcus</i> spp.	2 (4.2)	2 (5.4)
Sterile	39 (81.3)	12 (32.4)
Not done	5	16

representing 41.5% of all patients treated for PLA [Table 2].

All except two of the isolated *K. pneumoniae* were susceptible to usual antibiotics. One of the resistant

K. pneumoniae was carbapenem-resistant enterobacteriaceae (CRE) and the other extended-spectrum beta-lactamase (ESBL). Both were isolated in non-cryptogenic patients. One of these patients had pancreatic cancer, while the other had non-Hodgkin lymphoma and both of these patients died.

The majority of PLA patients (n = 46; 86.8%) were treated in the general ward, while the remaining seven (13.2%) were admitted directly to the intensive care unit due to sepsis. Out of these seven patients, three had urgent abdominal surgery. In 40 (75.5%) patients, ultrasound- or CAT-guided percutaneous abscess drainage was performed, after which the antibiotic treatment was continued. A total of 13 (24.5%) patients were treated only with antibiotics. The overall in-hospital PLA mortality rate was 9.4% (n = 5). Out of the five patients that died, two had pancreatic cancer, one had non-Hodgkin lymphoma, one was a post-liver transplant patient and one had cryptogenic PLA.

Discussion

PLA is an uncommon but potentially life-threatening disease with significant morbidity and mortality that varies around the globe. Regarding its geographical distribution, PLA is more often seen in Asia than in Europe or the USA.¹² The annual incidence per 100,000 inhabitants ranged from 1.1 in Denmark to 36.6 in Taiwan over the last two decades.¹³ At the same time, in the USA, the annual hospitalisation incidence due to PLA was 3.6 per 100,000 admissions.¹⁴ In this regard, as this study was based on a single-centre experience, it was not possible to estimate the PLA incidence in Oman.

It is well-known that the PLA incidence is higher in males than in females and the results of this study are concordant to this, as three quarters of the patients were male.¹⁵ Likewise, PLA is more often seen among the elderly population, where it might have an atypical clinical presentation; moreover, these patients do have more underlying diseases that can complicate the PLA clinical course.¹⁶ Nevertheless, the disease outcome in these patients is not significantly different when compared with younger PLA patients.¹⁷ In the current study, the patients were younger than those in other published reports, where the average age was usually around 65 years.^{18–20} Furthermore, in a few reports, the mean age as well as the majority of PLA patients were in the fourth decade of life.^{21,22}

PLA symptoms are non-specific and, thus, it is difficult to diagnose the disease based only on the clinical presentation. The majority of patients in this study complained of abdominal pain, with fever presenting less frequently, in 42 (79.2%) and 31 (58.5%)

patients, respectively. In other published reports, fever was usually the most common symptom followed by abdominal pain.^{5,22} However, Mangukiya *et al.* reported that in their patients, abdominal pain was the most common clinical sign.²³ The fact that the present study is retrospective in nature could explain why fever was not noted more frequently. The other reason could be that some of the patients were referred to the hospital under concern after the antibiotic treatment had already been started in their local hospital.

Previous studies indicated that comorbidities (diabetes mellitus, malignancies and liver cirrhosis), male gender, abscess size >5 cm and PLA complications (i.e. sepsis with or without organ failure, abscess rupture and extrahepatic involvement) are the risk factors that increase the PLA mortality rate.⁵ The mortality rate among the patients of the current study was 9.4%. One of the patients with a fatal disease outcome had cryptogenic PLA and being male was the only risk factor he had. The other four patients that died had at least two risk factors (malignancies, male gender, abscess size and/or sepsis with multiorgan failure), which increased the possibility of a fatal outcome.

In this study, *K. pneumoniae* was the most common cause of PLA. No anaerobic bacteria were isolated, although several studies reported that these bacteria are detected in 9–46% of PLA patients.²⁴ This is probably because anaerobic pus cultures were not routinely tested nor specifically requested. The *K. pneumoniae* predominance was shown as the cause of PLA, especially cryptogenic LA, in other studies.^{6,25,26} The first reports about the community-acquired PLAs caused by hypervirulent *K. pneumoniae* (hvKP) in Taiwan were published in 1986; now, the infection is recognised worldwide.²⁷ The typical presentation of hvKP infection is a cryptogenic PLA in a usually younger and previously healthy person. As hvKP has the tendency for metastatic spreading, these PLA patients can present with extra-hepatic abscesses, pneumonia, necrotising fasciitis, endophthalmitis and meningitis.²⁸ In the current study, two of the patients, both with cryptogenic PLA, had pleural effusions and necrotising pneumonia with consequent cavitory lesions. These patients were diabetic without any other comorbidities; one was 21 and the other 49 years old. The clinical presentations of these two patients strongly suggested that *K. pneumoniae* causing the infections in both cases were most probably hvKP, although no phenotyping nor molecular analysis was done to confirm this.

This study has various limitations. One of the limitations is that it was retrospective in nature, so the results should be interpreted with caution. Moreover,

microbiological analysis was only partly done, thereby disregarding the proper anaerobic pus sample cultures. Furthermore, as this study covered a single-centre experience, the results do not represent the overall PLA situation in Oman.

Conclusion

This study provides important information about PLA characteristics, at least with regard to the northern part of Oman. Presenting symptoms were non-specific, indicating that in patients with abdominal pain and fever, the differential diagnosis process should include LA. The majority of PLAs were caused by *K. pneumoniae*, therefore, the empirical treatment should be started with antibiotic directed against it. Further studies are needed to establish the local role of anaerobic bacteria in PLA and monitor the presence of hvKP in Oman.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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AUTHORS' CONTRIBUTION

NP conceived and designed the study, also drafted the manuscript. ASM and AM collected the data and performed the data analysis. MM and SSD performed the final data analysis. FK and ZB supervised the data analysis. All the authors contributed to the revision of the manuscript. All authors approved the final version of the manuscript.

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