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Characteristics of Pyogenic Liver Abscess

Experience of a Single Centre in Oman

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Abstract

Objectives: Liver abscess 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. The goal of this study was to analyze the epidemiology, etiology and clinical characteristics of pyogenic liver abscess in Oman. The intention was to obtain the information needed for the adequate liver abscess empirical treatment. **Methods:** This retrospective study took place in a tertiary hospital. Consecutive patients treated for the liver abscess during the five years period, from January 2013 until the end of 2017, were enrolled. Their demographic and clinical data were used to study the characteristics of pyogenic liver abscess in Oman. **Results:** Fifty-three patients with pyogenic liver abscess were enrolled in the study. They were predominantly male and younger than 60 years. *Klebsiella pneumoniae* was the most usual bacteria causing the liver abscess. Clinical presentation was unspecific and the abdominal pain and high fever were the most usual symptoms. **Conclusion:** The majority of pyogenic liver abscesses are caused by *K. pneumoniae* so the empirical treatment should be started with antibiotic directed against it. Further studies are needed to establish the local role of anaerobic bacteria in pyogenic liver abscess as well as to monitor the presence of hypervirulent *K. pneumoniae* in Oman.

Keywords: Pyogenic liver abscess; Etiology; Epidemiology; *Klebsiella pneumoniae*.

Advances in Knowledge

- This study is the first study analyzing the clinical, epidemiological and etiological aspects of pyogenic liver abscess in Oman.
- *Klebsiella pneumoniae* is the most common cause of pyogenic liver abscess in Oman.
- The majority of patients have the cryptogenic form of liver abscess.

Application to Patient Care

- Identifying the pyogenic liver abscess characteristics in Omani population will help the healthcare practitioners to plan the appropriate differential diagnosis workup as well as starting the adequate empirical treatment.

Introduction

Liver abscess (LA) is defined as an encapsulated collection of pus within the liver parenchyma. The majority of LAs are caused by bacteria generating a pyogenic liver abscess (PLA) while parasites and fungi are less common LA causes.¹ During the early years of 20th century PLA was seen most often secondary to appendicitis but later on, biliary tract diseases usually precede the PLA.² More recently PLAs can be associated with secondary infection of a primary liver tumor or metastatic liver lesions as well as their treatment, particularly as complications of trans-arterial chemoembolization or radiofrequency ablation.^{3,4} In the situation where following full investigation, no obvious source of extra-hepatic infection was determined the PLA is labeled as cryptogenic.⁵

The prevalence of cryptogenic PLAs varies throughout the world. In the United Kingdom and France, it is about 17%, Australia 34% respectively, while in Asia it reaches 65%.⁶ Previous studies showed a significant difference in PLA etiology. In Europe and North America *Escherichia coli* (*E. coli*), *Staphylococcus* spp, *Streptococcus* spp. and *Enterococcus* spp. are the most common causes of PLA while in Asia the predominant bacteria causing PLA is *Klebsiella pneumoniae* (*K. pneumoniae*).⁷ Several studies showed that *K. pneumoniae* is the main cause of cryptogenic PLA regardless geographical distribution.^{6,8} The characteristics of PLA in Gulf countries are not well known. As per the authors' knowledge, one study from Qatar and few case reports from Oman and KSA describing PLA were published so far.⁹⁻¹¹

The aim of this retrospective study was to establish the epidemiological and clinical characteristics of PLA in Oman.

Methods

The study was conducted in The Royal Hospital, Muscat, Oman after the approval from the Royal Hospital Scientific Research Committee. The patients' data were collected from the Royal Hospital data base. All the patients older than 13 years that were treated for the LA during the period from January 2013 until the end of 2017 were enrolled in the study. The liver abscess etiology was determined by abscess and/or blood culture. The blood for the aerobic and anaerobic culture was taken at the 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 IgG anti-amoebic assay. Patients with confirmed amoebic liver abscess were excluded from the study. In order to trace a possible but undetected underlying PLA source during the hospitalisation, after the discharge, the patients were followed up through the hospital database system during the period from one to six years.

Results

During the five years period 76 patients were treated for the LA. Out of this number, 53 patients had PLA while the remaining 23 had amoebic LA so they were excluded from the analysis. Forty patients were male (40/53; 75.47%) and 13 (24.53%) were female. The mean age of the whole group was 46.8 years (range 14 to 92 years). When comparing the average age of male and female patients there was no statistical difference although the mean age for the male patients was 51.3 years and for the females 44.7 years. The clinical presentation of PLA was very unspecific and upper abdominal pain was the most common symptom found in 42 (79.3%) of our patients. Fever was present in 31 patients (58.5%) and on examination 13 (24.5%) patients were icteric. At the admission to the hospital 34 (64.2%) patients had leukocytosis above $10 \times 10^9/L$ (reference range: $2.4 - 9.5 \times 10^9$). Alanine aminotransferase (ALT) above 40 IU/L (reference range: 0 – 40 IU/L) was found in 30 (56.6%) and bilirubin above 20 mmol/L (reference range: 0 – 20 mmol/L) in 18 (34.0%) patients.

The definite PLA diagnosis was established by CAT scan, MRI or abdominal ultrasound. Thirty-five (66.0%) of our patients had a single abscess. Most often, in 33 patients (62.3%), the PLA was found in the right liver lobe. In 13 (24.5%) patients it was in the left lobe while

in 7 patients (13.2%) 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 our patients, 34 (64.2%) had cryptogenic PLA. The diseases that preceded PLA in our patients are presented in the Table 1.

Blood and/or abscess culture were positive in 30 (62.3%) patients while in the rest 23 PLAs etiology was not determined because the cultures remained sterile. *K. pneumoniae* was the most common bacteria causing PLA and it was found in 21 patients representing 39.6 % of all patients treated for the PLA. The bacteria causing PLA in our patients is presented in the Table 2. All but two of the isolated *K. pneumoniae* were susceptible to usual antibiotics. One of the resistant *K. pneumoniae* was CRE and the other ESBL. Both were isolated in patients from non-cryptogenic group. One of these patient had pancreatic cancer while the other had non-Hodgkin lymphoma, and both of these patients died.

The majority of PLA patients (86.8%) were treated in general ward while the remaining 7 (13.2%) were admitted directly to the ICU due to sepsis. Out of these 7 patients, 3 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. 13 patients (24.5%) were treated only with antibiotics. The overall in-hospital PLA mortality was 9.4% (N=5). Out of five patients that died, two had pancreatic cancer, one had non-Hodgkin lymphoma, the fourth was the post-liver transplant patients and one patient had cryptogenic PLA.

Discussion

PLA is an uncommon but potentially life-threatening disease with significant morbidity and mortality that varies around the globe. Regarding the world geographical distribution, PLA is more often seen in Asia than in Europe or Americas.¹² The annual incidence per 100,000 inhabitants ranges from 1.1 in Denmark to 36.6 in Taiwan.¹³ At the same time, in the USA, the annual hospitalization incidence due to PLA was 3.6 per 100,000 admissions.¹⁴ As this study is a single centre experience it is not possible to assume the PLA incidence in Oman.

It is well known that the PLA incidence is higher in males than in females,¹⁵ and the results of our study are concordant to this as three quarters of our patients were males. Likewise, PLA is more often seen in the elderly population where it might have an atypical clinical presentation

and also, these patients do have more underlying diseases that can complicate the PLA clinical course.¹⁶ Nevertheless, the disease outcome is not significantly different when compared with younger PLA patients.¹⁷ In our study the patients are younger than those in other published reports where the average age was usually around 65 years.¹⁸⁻²⁰ At the same time there are reports showing that the mean age as well as the majority of PLA patients were in the fourth decade of life.^{21,22}

PLA symptoms are very non-specific and it would be extremely difficult to diagnose the disease based only on the clinical presentation. The majority of our patients complained of the abdominal pain which was present in 42 (79.2%) cases. Fever was present less frequently and it was reported in 31 (58.5%) patients. In other reports published so far, fever is usually the most common symptom followed by the abdominal pain,^{5,22} yet Mangukiya and coauthors reported that in their patients the abdominal pain was the most common clinical sign.²³ As our study is the retrospective one, this could be the explanation why fever was not noted more frequently, and the other reason could be that some of our patients were referred to our hospital after the antibiotic treatment was already started in their local hospital.

Previous studies indicated that comorbidities (diabetes mellitus, malignancies and liver cirrhosis), male gender, abscess size >5cm, 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 in our patients was 9.4%. One of the patients with the fatal disease outcome had cryptogenic PLA and male gender was the only risk factor he had. The other 4 patients that died had at least 2 risk factors that increased the possibility of fatal outcome: malignancies, male gender, abscess size and sepsis with multiorgan failure.

In our study *K. pneumoniae* was the most often cause of PLA while the other bacteria were less frequently found. There were no anaerobic bacteria isolated although several studies reported that these bacteria are detected in 9% - 46% of PLA patients.²⁴ Most probably the reason for this is that anaerobic pus cultures were not routinely tested nor specifically requested. The *K. pneumoniae* predomination as the cause of PLA is shown in other studies, especially in cryptogenic liver abscess.^{6,25,26} The first reports about the community acquired PLAs caused by hypervirulent *K. pneumoniae* (hvKP) in Taiwan were published in 1986, but since that time the same infection is recognized worldwide.²⁷ The typical presentation of

hvKP infection is a cryptogenic PLA in usually younger and previously healthy person. As hvKP has the tendency for metastatic spreading, these PLA patients at the same time can present with extra-hepatic abscesses, pneumonia, necrotizing fasciitis, endophthalmitis, and meningitis.²⁸ Interestingly, the two of our patients, both with cryptogenic PLA, had pleural effusions and necrotizing pneumonia with consequent cavitory lesions. They were diabetic patients without any other comorbidities. One was 21 and the other 49 years old. The clinical presentation of our two patients strongly suggest that both *K. pneumoniae* causing their infections most probably were 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 a retrospective one so the results should be interpreted with caution. The other limitation is that microbiology analysis was only partly done missing the proper anaerobic pus sample cultures. As this is one centre experience, the results do not represent the overall PLA situation in Oman.

Conclusion

Although with limitations, this study gives an important information about PLA characteristics at least in the northern part of Oman. Presenting symptoms are nonspecific indicating that in patients with the abdominal pain and fever the differential diagnosis process should include liver abscess. The majority of PLA are caused by *K. pneumoniae* so 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 as well as to monitor the presence of hvKP in Oman.

Conflict of Interest

The authors declare no conflicts of interest.

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Table 1: Demographic and clinical characteristics of PLA patients.

	No	%
Female	13	24.5
Male	40	75.5
Age <60 years	36	67.9
Age >60 years	17	32.1
Symptoms		
Fever	31	63,16
Abdominal pain	42	89,47
Jaundice	13	26,32
Laboratory results		
WBC >10	34	64.2
ALT >40	29	54.7
Comorbidities		
Hepatobiliary disease	17	32.1
Immunosuppression	3	5.7
Intraabdominal trauma	1	1.9
Diabetes mellitus	15	28.3
None	12	22.6

Table 2: Etiology of pyogenic liver abscess

	Blood culture (N=48)		Abscess culture (N=37)	
	N	%	N	%
<i>K. pneumoniae</i>	5	9.4	17	46.0
<i>E. coli</i>	1	1.9	3	8.1
<i>Enterococcus</i> spp.	1	1.9	1	2.7
<i>P. aeruginosa</i>	0	0	1	2.7
<i>S. aureus</i>	0	0	1	2.7
<i>Streptococcus</i> spp.	2	3.8	2	5.4
Sterile	39	73.6	12	32.4
Not done	5		16	