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The Pyogenic Hepatic Abscess: To Drain or not to Drain, that is the Question. Clinical Presentation and Outcome Evaluation after Conservative and Invasive Treatment

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Abstract

Background: Pyogenic hepatic abscess (PHA) is an uncommon infectious disease of the liver that should represents a life-threatening condition if not correctly diagnosed and managed. Nowadays there are not precise indications and clear evidences on the best therapeutic approach and on the superiority of a treatment.

Methods: Patients with diagnosis of PHA admitted at the Policlinico "Paolo Giaccone" at Palermo University Hospital between January 2010 and December 2022 were identified in a prospective database. Among the demographic, epidemiological and clinical data collected we included the therapeutic choices – antibiotic treatment, image guided percutaneous drainage and surgical operation – and their effect in terms of healing time, treatment failure and time of hospitalization.

Results: Patients with single abscesses treated with antibiotics have significant high healing time (p=0.0001) and in-hospital time (p=0.0001) and no differences in treatment failure than patients treated with invasive techniques. Patients that underwent surgical operation have significant higher healing time than percutaneous group (p=0.002) such as higher mean hospital stay (p=0.03 for abscesses <5 cm and p=0.02 for abscesses larger than 5 cm). The last, the percutaneous approach shows a failure rate significantly higher than the surgical procedure (p=0.009 for abscesses <5 cm and p=0.001 for abscesses larger than 5 cm).

Conclusions: The study proposed showed the antibiotic therapy is the first line treatment and should first empirically and then directly modified on specimen culture results. Image guided percutaneous drainage should be considered when the antibiotic therapy alone is not sufficient or as bridge to surgery if surgical indications are proven.

Keywords: Pyogenic Hepatic Abscess; Clinical presentation; Antibiotic treatment; Percutaneous drainage; Outcome evaluation.

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Introduction

The hepatic abscess (HA) is an infectious disease characterized by a capsule collection with a suppurative content in the context of the hepatic parenchyma, whose nature may be of bacterial, fungal and/or parasitic origin [1,2]. It represents an extremely severe and potentially fatal condition with an incidence rate ranging from 6 to 15% [3-5]. The incidence of the disease varies according to the geographical location of reference, with a clear difference between East and West. Recent studies have shown that in Europe and America the hepatic abscess presents with 1.1-3.6 cases per 100,000 inhabitants, while in Asia there is a rate of 17.6 cases per 100,000 inhabitants [6-8]. Nevertheless, it is considered an uncommon cause of liver disease [9,10].

The etiology is mainly of bacterial and amoebic nature, although other microorganisms such as fungi or Cytomegalovirus (CMV) can cause abscesses, above all in extremely selected patients such as in immunocompromised ones. Among the most common aerobic bacteria there are Klebsiella spp, E. coli and the Enterococci spp; while among the anaerobic bacteria the greatest percentages concern the Bacteroides spp, the Streptococci spp and the Fusobacteria spp [10]. The HA is often associated to complications of the biliary tract diseases in an estimated percentage of 40% of the cases, even though the most of the patients have not clear risk factors, defining the group of the cryptogenic abscesses. The amebic abscess is also common in young adult males and tends to present as a single solitary mass in the right liver lobe, while the pyogenic abscess is more common in adults over the age of 50 and often presents with multiple injuries [11-13]. Although significant progresses have been made in diagnosis and treatment of the hepatic abscess, it remains one of the major challenges in the field of the abdominal surgery and of the infectious diseases since the presentation may be not specific and the treatment not always resolutive [14,15].

Even though it is an uncommon pathology it represents a life-threatening condition if not correctly treated. Major risk factors for mortality include male gender, malignant etiology, multi-organ failure, rupture of the abscess, respiratory distress, hypotension, jaundice, extra-hepatic involvement, diabetes, sepsis and the dimension of the abscess [16]. The mortality for individuals with cancer is twice that of cancer-free patients, whereas cirrhotic patients have a 4-fold higher risk [17-18]. Early diagnosis and correct treatment are fundamental steps in the management of the disease in order to achieve the best outcome. This study aims to investigate [1] the clinical and radiological characteristics that allow to speed up the diagnostic timing and the characterization of the pyogenic hepatic abscess (PHA), and [2] to identify the therapeutic choice with the best outcome in an international scenario in which there is not a unique approach still now.

Material and methods

Patients with diagnosis of HA admitted at the Policlinico "Paolo Giaccone" at Palermo University Hospital between January 2010 and December 2022 were identified in a prospective database, and the data collected were retrospectively reviewed. Amebic HA were excluded from the study. Patients' medical records were collected from the charts. The diagnosis of PHA was obtained after physical examination, radiological tests - ultrasound/CT and/or MRI scan - blood exams and microbiology tests on blood or abscess specimens.

Data collection included demographic characteristics, etiological factors, clinical signs and symptoms, laboratory and radiological data, number, size and location of the lesions, microbiological findings, treatment approach and its effect. The infectious etiology and the antibiotic susceptibility tests were evaluated by culture examination on material taken from the abscess specimens and/or on blood. The abscess was considered secondary to biliary tract disease if cholecystitis or cholangitis occurred. It was considered secondary to hematic spread if different infectious source was discovered. The definition of "cryptogenic abscess" was attributed to the cases in which the clinical information and the microbiological data collected were not sufficient to define the etiopathogenetic origin of the lesion. Antibiotic therapy was first empirically and then directly introduced after the results of the cultures. Antibiotics were immediately started after collection of microbiological specimens obtained from abscess puncture and/or blood cultures, to control ongoing bacteremia and its associated complications. According to local epidemiology and resistance showed by the bacteria, initial empiric broad-spectrum parenteral antibiotic therapy was administered pending the results of the susceptibility tests.

Image-guided percutaneous drainage was performed in the radiology department; its indications were abscesses >3 cm and/or medical treatment failure. Surgical drainage was performed in surgical room, during the surgical operation proposed to treat the underlying cause of the abscess formation or after the failure of the conservative and/or image-guided approach.

Contraindications for invasive approach, both image-guided and surgical drainage, were small size of the abscess (<3 cm), clinical improvement after conservative therapy and poor clinical general conditions.

Treatment responsivity was evaluated through the progressive reduction of the disease indexes – WBC count, WBCs types percentage, procalcitonin (PCT), erythrocyte sedimentation rate (ESR), positive acute-phase proteins such as C-reactive protein (CRP), coagulation factors and ferritin - and the attenuation of the symptoms. Failure of the treatment was defined as the persistence of the signs, symptoms and laboratory findings of infection after one week of its beginning. Healing has been defined as the complete disappearance of signs and symptoms of disease.

In order to identify the best therapeutic approach, we wanted to conduct an investigation on the possible superiority of a treatment between the proposed ones. The cases were classified into three classes: A) single abscesses <5 cm; B) single abscesses >5 cm and C) multiple abscesses without dimension characterization. The parameters used to test the possible superiority of a conservative medical approach instead of the invasive percutaneous or surgical approach were 1) mean time of healing; 2) failure of the treatment, stated through the absence of improvement on clinical, serological and radiological findings after the treatment proposed; 3) mean time of hospitalization.

Follow-up was performed for at least one year. After discharge from the hospital, all patients were examined weekly during the first month, monthly for 6 months and then annually. The follow-up consisted of the physical examination, the WBC count with WBCs types' percentage, and US abdominal scan when necessary. Data were analyzed in Excel 2016 and IBM SPSS software, version 21. The mean and median were obtained for continuous variables. Comparisons of continuous variables were made using Student's t test or the Mann–Whitney test where appropriate. A comparison of categorical variables was made with the Chi-squared (χ^2) test or Fisher's exact test. The statistical significance level was set to a pvalue <0.05. All methods were carried out in accordance with relevant international guidelines after obtaining the informed consent from all subjects. Approval by the Regional Ethics Review Board in Palermo was obtained in order to conduct the study (ID number 0020192).

Results

Between January 2010 and December 2022, a total of 76 patients were admitted to the Policlinico "Paolo Giaccone" Hospital with the diagnosis of PHA and included in the study. 44 patients (58%) were males and 32 patients (42%) were females. The age ranged from 33 to 94 years, with a mean of 69 years (SD±17). The most common symptom was fever in 27 cases (35.5%), followed, in decreasing progression, by pain in the right hypochondrium in 19 cases (25%), jaundice in 13 cases (17%), nausea and vomiting in 10 cases (13%), chills in 6 cases (8%), weight loss in 6 cases (8%) and finally asthenia in 5 cases (6.5%). The analysis of the comorbidities showed that 52 patients (68.4%) had hypertension; 30 patients (39%) presented with uncontrolled diabetes mellitus; thirteen patients (17%) presented with cholangitis, 9 patients (12%) with acute cholecystitis, 4 patients (5.2%) with cholangiocarcinoma, and one patient (1%) with hepatocellular carcinoma (HCC). There were also 3 patients (3.9%) with chronic renal failure and one patient with metastatic adenocarcinoma of the right colonic flexure.

The laboratory data showed the increase of all the inflammatory indexes and particularly the elevation of CRP in 67 cases (88%) and of the ESR in 70 cases (92%). In association with these parameters the increase in WBC count was found in 60 cases (79%), bilirubin in 23 cases (30%) and transaminases in 15 cases (20%). Altered fibrinogen blood levels was found in 32 patients (42%), PCT elevated values in 15 patients (20%) and hypoalbuminemia in 17 patients (22%).

Abdominal ultrasound was found to be diagnostic in 34% of cases; CT-scan of abdomen was performed in 72% of cases. Only 4 patients (5%) underwent MRI (see Table 1). By analyzing the site where abscesses developed, they can be roughly distinguished in lesions affecting the right hepatic lobe and lesions affecting the left hepatic lobe with a 3:1 ratio. Among all abscesses, 56 (74% of cases) were identified within the right lobe, while 18 (24% of cases) in the context of the left lobe. Only 2 patients (2%) had bilateral localization. The abscesses were also distinguished by the number of lesions in single or multiple; 85.5% of cases (65 patients) had a single abscess, whose mean size was 9.6 cm (range 3.5-20 cm) SD±5.3. Of these patients, 50 (66%) showed lesions <5 cm, while 15 (20%) had lesions >5 cm in diameter. In 5 cases there were 2 abscesses with a mean diameter of 7.8 cm (range 2.7-15 cm) SD±5.1. Finally, 8% of cases (6 patients) showed multiple abscesses with a mean diameter of 4.4 cm (range 1.5-7 cm) SD ± 5.3.

Microbiological data were obtained starting from the culture on a sample taken from the abscess during the drainage and/or from blood culture. These were positive for 59 patients, while 17 cases were negative. The most common organism identified was E. coli in 28 cases (37%), followed by Enterococcus in 10 cases (13%), K. pneumoniae in 7 cases (9%) and Streptococcus in 5 cases (6.5 %). Other microorganisms were P. aeruginosa (4%) and Proteus (8%). The empiric antibiotic therapy was the first choice of treatment in all patients although only in 35 cases (46%) it proved to be sufficient for the eradication of the microorganism and the achievement of the expected outcome. The antibiotic therapy was then changed with target therapy after the antibiotic susceptibility tests were performed. The mean time of the antibiotic therapy was 17 days (SD±3.9).

Twenty-four patients (31.6%) were treated by percutaneous image-guided drainage. A percutaneous French 7 pigtail catheter was inserted in order to drain the abscess. The removal of the drainage was based on the response of the patient on clinical and laboratory findings. The mean time of drainage duration was 7±3 days. Seventeen patients (22%) benefited from the surgical approach whose indications were the eradication of the etiopathogenetic noxa identified as cause of the abscess formation or failure of the previous treatment choices (see Table 2). The analysis conducted to verify if a treatment should be proposed as superior than the others, showed that for both the single abscesses classes, the mean healing time in conservative group that was respectively 14 d and 16 d were higher that the invasive groups, respectively 6 d and 10 d with p=0.0001 for both the comparisons performed. Moreover, the mean hospitalization time was respectively 18 d and 21 d for conservative groups compared to 6 d and 10 d of the invasive groups with a p=0.0001.

No differences were observed in failure of the treatment amongst the two classes. No significative differences were observed between the treatment options in the class of multiple abscesses (see Table 3). Similarly, we conducted the analysis between the surgical and the percutaneous approach in the classes of single abscess divided by dimension. The parameters considered were the same used before. The analysis conducted showed that for the single abscess >5 cm class the healing time was significantly higher in surgical group (7 d vs 4 d; p=0.002) such as the mean hospitalization time for both the single abscess classes: in single abscess <5 cm we found 6d vs 3d with p=0.03, and in single abscess >5 cm we found 8d vs 5 d with p=0.02. The last, the failure of the treatment was found significantly higher in the image-guided approach versus the surgical approach in both the classes with 5 vs 0 failed patients with p=0.009 and 4 vs 0 failed patients with p=0.01 respectively (see Table 4). Five patients died during the hospital admission, resulting directly from the abscess and its complications. All of them were patients admitted with signs of sepsis and multi organ failure that died within a mean in-hospital stay of 3 days (SD±2.6).

Table 1: Demographic data.

Age (mean; SD)	**69 ± 17**
Sex	
M (%)	58
Comorbidities	
Hypertension (%)	68.4
DM type 2 (%)	39

Cholangitis (%)	17
Acute cholecystitis (%)	12
Cholangiocarcinoma (%)	5.2
Chronic renal failure (%)	3.9
Hepatocellular carcinoma (%)	1
Metastatic colonic adenocarcinoma (%)	1
Symptoms	
Fever (%)	35.5
Right hypochondrium pain (%)	25
Jaundice (%)	17
Nausea and vomiting (%)	13
Chill (%)	8
Weight loss (%)	8
Asthenia(%)	6.5
Laboratory indexes alteration	
C-reactive protein (%)	88
Erytrocite sedimentation rate (%)	92
WBC count (%)	79
Bilirubin (%)	30
Transaminases (%)	20
Fibrinogen (%)	42
Procalcitonin (%)	20
Hypoalbuminemia (%)	22
Radiological diagnosis	
Ultra sound (%)	34
CT scan (%)	72
Magnetic resonance (%)	5

Table 2: Abscess characteristics.

Right hepatic lobe (%)	74
Left hepatic lobe (%)	24
Bilateral hepatic lobe (%)	2
Single abscesses (%)	85.5
Mean size (cm)	9.6
SD	±5.3
Lesion < 5 cm (%)	66
Lesion > 5 cm (%)	20
Multiple abscesses (%)	8
Mean size (cm)	4.4
SD	±5.3
Epidemiology	
E. coli (%)	37
Enterococcus spp (%)	13
K. pneumoniae (%)	9
Proteus spp (%)	8
Streptococcus spp (%)	6.5
P. aeruginosa (%)	4
Treatment modalities	
Antibiotic therapy (%)	100
Percutaneous image-guided drainage (%)	32
Surgical approach (%)	22

Table 3: Outcome evaluation and comparison between medical and invasive treatment.

	Single abscess <5 cm			**Single abscess >5 cm**			**Multiple abscesses**		
	Medical treatment	Invasive treatment	p-value	Medical treatment	Invasive treatment	p-value	Medical treatment	Invasive treatment	p-value
Healing time (days) SD	14±1.5	6±1.7	0.0001	16±3.1	10±0.9	0.0001	17±3.9	13±2.6	0.07
Treatment failure (number of patients)	9	5	0.36	4	2	0.2	2	6	0.7
Mean hospitalization time (days) SD	18±2.6	6±1.8	0.0001	21±2.6	10±3.2	0.0001	24±2.8	2.2±1.7	0.17

Table 4: Outcome evaluation and comparison between surgical approach and image guided drainage.

	Single abscess <5 cm			**Single abscess >5 cm**		
	Surgical approach	Image guided drainage	p-value	Surgical approach	Image guided drainage	p-value
Mean healing time (days) SD	5±3.6	3±2.5	0.16	7±2.5	4±0.8	0.002
Treatment failure (number of patients)	0	5	0.009	0	4	0.01
Mean hospitalization time (days) SD	6±3.9	3±2.1	0.03	8±2.3	5±1.2	0.02

Discussion

The study proposed aimed to investigate the characteristics of clinic, etiology, microbiology and treatment of the hepatic abscess, and to verify the superiority of a treatment approach upon the others. The PHA remains still now a rare multifactorial disease that should represents a life-threatening condition if not correctly diagnosed and treated.

The clinical presentation is extremely variable and characterized by the presence of poorly specific symptoms. Among the most representative manifestations we found fever, pain in the right hypochondrium, jaundice, nausea and vomiting. The clinical findings are often associated with the elevation of the inflammatory indexes - such as WBC count and WBCs type percentage alteration, CRP, ESR, fibrinogen and PCT - and the elevation of hepatic indexes such as bilirubin and transaminases. Moreover, the diagnostic hypothesis is often supported by the

presence of predisposing conditions of abscess formation, such as biliopancreatic pathologies present in 35.2% of the cases, despite the increasing number of cryptogenic lesions that in our study rises the 22.3% of the cases similarly to the case series presented by Serraino et al. [19].

Diagnostic confirmation was obtained by imaging of the liver. Ultrasonography is a diagnostic possibility because it is non-invasive and has no side effects, since it does not include exposure to radiation. It also allows for the differential diagnosis between solid lesions and cystic lesions, characterizing the vascularization through the use of the doppler. Ultrasound alone was the diagnostic investigation in 34% of the cases. The CT-scan of the abdomen was vice versa the main choice, performed in 72% of the cases. 6% of the patients who performed the US-scan, needed for the CTscan integration for a differential diagnosis. Magnetic resonance has a marginal role, performed in only 5% of the cases after CT-scan execution, and it is limited to cases in which it was indicated the study of the intrahepatic biliary tree. Radiological findings showed the prevalence of abscess localization in right hepatic lobe. Also Ruiz-Hernàndez et al. [20] presented the same scenario and this should be due to the specific anatomy of the portal vein trunk and the major hepatic mass in the right lobe.

The microbiological investigation was performed routinely to all the patients and in 77.6% it was isolated the microorganism responsible of the abscess formation. The microbiological data were obtained by analysis performed on samples taken from the abscess and/or on blood culture. The pathogens found in the culture of the study are perfectly comparable to those presented in other European series that are epidemiologically comparable [21]. A higher incidence of infections sustained by E. coli was observed with a percentage of 37%. The other main pathogens were Enterococcus and K. pneumoniae, respectively in 13 and 9% of the cases. The cases associated to K. pneumoniae seem surprisingly high compared to the European series which cases are approximately 5.6% [21].

Antibiotic therapy was the first choice of treatment in all patients, although only in 35 cases (46%) proved to be sufficient for the eradication of the microorganism and the achievement of the expected outcome. According to local resistance epidemiology, fluoroquinolones, third and fourth generation cephalosporins, piperacillin/tazobactam, aminoglycosides and carbapenems remain effective treatment options for pyogenic abscesses. The antibiotic therapy was generally used as the only therapeutic choice for abscesses smaller than 5 cm in diameter. The same approach was recently published by Lardière-Deguelte S et al. [2] with a success rate for HA over 80%. In 2008, Hope et al. reported a 100% success rate with antibiotic therapy alone for unilocular HA <3 cm in their series of 107 patients [22]. Similarly, in a literature review of 465 medically-treated abscesses, 176 of which were located in the liver, the 5 cm cut-off was the main factor associated with success of medical treatment alone [23].

On the other side, when a poor or absent response to antibiotic treatment is obtained or a diagnosis of major hepatic lesion is made, image-guided drainage is considered the best therapeutic choice. Ferraioli et al. [24] demonstrated that if radiology is readily available, surgical drainage is rarely indicated. However, for some authors, there is a role for surgical drainage if percutaneous treatment for HA fails, for large abscesses >5 cm, and/or multilocular HA, or when surgical treatment of the underlying cause of HA is necessary [25,26].

In our experience the surgical approach was indicated in only 17 subjects (22%) for treatment of the underlying cause of HA and contemporary drainage of the abscess. The study conducted shows the superiority of the invasive treatment on the conservative one in terms of mean time of healing and mean time of hospitalization for single abscesses groups. This evidence must therefore be carefully considered because of it is not always possible to indicate the image guide or the surgical approach for the above-mentioned reasons, such as too small lesions, poor clinical conditions of the patient or coagulation alterations. It should be considered a tailored approach on the basis of the comorbidities and of the clinical presentation of the disease. On regard of the single abscess larger than 5 cm the surgical approach seems to be superior to image guided percutaneous drainage in terms of number of failed procedures, even though mean healing time and mean in-hospital stay are in advantage for the image guided technique. The mortality rate was 6.6% similar or a little lower than other reports such those of Kuo et al. [5], Ruiz-Hernandez et al. [20] and Verlenden et al. [27] and. The causes remain sepsis and/or septic shock in patients with poor clinical conditions.

Conclusions

The study aimed to show the characteristic of the PHA presentation in a high-volume metropolitan hospital, in order to provide information on the clinical manifestations, the underlying diseases responsible of PHA formation, microbiology epidemiology, treatment approaches and their results. Though aware of the various spectrum of clinical presentations and of the comorbidities that should impair the general conditions, we believe that the surgical approach, when performable, has the minor failure risk than other techniques and should be considered curative if the underlying cause of PHA formation is known (e.g. biliopancreatic disease, etc.). The antibiotic therapy is the first line treatment and should empirically introduced to every case of HA with the possibility to change it if necessary and if susceptibility tests are performed on specimens. Image guided percutaneous drainage should be considered when the antibiotic therapy alone is not sufficient or as bridging therapy to surgery if surgical indications are proven. Moreover, the percutaneous drainage should be the treatment of choice if poor general clinical conditions are stated or if cryptogenic PHA is diagnosed.

Declarations

Ethics approval and consent to participate: Not applicable

Consent for publication: Not applicable

Availability of data and material: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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