

Liver abscesses: etiologic factors and diagnostic errors

A. D. Zubov, J. I. Wilson

Donetsk National Medical University n. a. M. Gorky

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Liver abscesses (LA) are a group of serious diseases of various etiologies, characterized by the presence of a limited accumulation of pus on the background of the hepatic parenchyma destruction, resulting from the penetration of microbial flora or parasites [3]. LA frequency is high (0.08-2% of hospitalized patients), and not only has a tendency to decrease, but, according to some authors, significantly increases [2, 4, 6, 7, 9].

There are many classifications of LA based on their clinical course, etiology, pathogenesis, number and location of foci. There are several ways of spreading the infection to the liver: through the portal vein; through the bile ducts; through the hepatic artery; mixed; upon the liver injury; the direct spread of infectious-inflammatory process from nearby organs, which form the basis of a number of LA classifications. The best known is the classification of non-parasitic LA according to Meyers (2001) [1, 14], including: cryptogenic LA, cholangiogenous (of benign and malignant origin); intestinal (of benign and malignant origin), other portal (except for intestinal) hematogenous (blood), liver injury, other (chronic granulomatosis, local spread, abdominal surgeries, etc.). In clinical practice, a differentiated approach to these liver suppurations determines differentiated tactics of their treatment. However, there is no consensus in the literature concerning the prevailing causes and risk of LA development, which requires further studying. In particular, there is no mention of the role of intestinal diseases in the genesis of LA.

The main causes of adverse outcomes of inflammatory processes in the abdominal cavity are associated with delayed diagnostics [5]. Since LA polyetiology causes clinical polymorphism, it is extremely difficult to diagnose LA, evaluate its

location and spread by only physical methods of research. Therefore, instrumental diagnostic methods play a leading role in verification of this pathology [5, 11].

However, LA often take place under the guise of another clinical disease [8, 10]. It is specified that LA may show symptoms of diseases of the pleura, lungs, organs of pelvic and retroperitoneal space, pancreas, depending on the localization of the pathological process [1, 5, 12]. Being mainly in the departments of therapeutic profile, such patients receive treatment for misdiagnosed disease, while methods of radiological imaging (US, CT) are used upon a significant deterioration in the condition of the patient. However, data on the causes of diagnostic errors and the ways to minimize them are few and fragmented in the literature. In this connection it is relevant to study the role of the US as a high-quality, affordable and harmless method to minimize the risk of diagnostic errors.

The aim is to study the main etiological factors of the LA development and to formulate recommendations for the precision liver ultrasound to detect signs of possible abscess formation.

Materials and methods

Studies were conducted on the basis of clinical specimens of 248 patients of both sexes aged from 4-81 with LA, the average age was 48.0 ± 13.6 . The study excluded patients with LA of parasitic origin (amoebic, opisthorchosis, festering echinococcus cysts), as well as with postoperative bilomas.

Anamnestic, physical, clinical and laboratory tests were carried out. In collecting a medical history, existing or recent illnesses of abdominal organs were taken into account: large intestinal, diverticulitis, Crohn's disease, bacterial colitis, acute appendicitis, appendiceal abscess, cancer of the gastrointestinal tract, cholelithiasis, choledocholithiasis. Intake of proton pump inhibitors for two or more months was recorded in the history. Biliary and liver surgeries, external or internal stenting of the bile duct, surgery on other organs, injuries were taken into consideration. LA were classified on the basis of ways of infection penetration in the liver.

To identify the bacterial overgrowth syndrome (BOS), 76 patients including 40 with pylephlebitic and 36 with posttraumatic LA, underwent a hydrogen breath test EC 60 Gastrolyzer 2.

The diagnosis of LA was verified echographically, upon CT, as well as in performing medical procedures (needle aspiration or drainage under ultrasound guidance). Ultrasound was performed in all patients on the scanners AI-5200, HDI 5000, Logic 3, Aplio 500 with convex probe 3.5-5.0 MHz.

The results were processed using conventional statistical methods. The average and error of the mean were calculated, the comparison of unit shares was carried out by χ^2 method corrected for small sample.

Results and discussion

LA ratio of various etiologies is shown in Fig. 1. It is noted that the distribution of LA according to etiology in the study group is not consistent with the literature data. According to most authors, cholangiogenous LA have represented the main etiological group for the last 25 years [1, 2, 9, 13]. However, in this study, which included all patients examined and treated in a regional hospital from 2005 to 2014, the main part (64.1%) was represented by pylephlebitic LA.

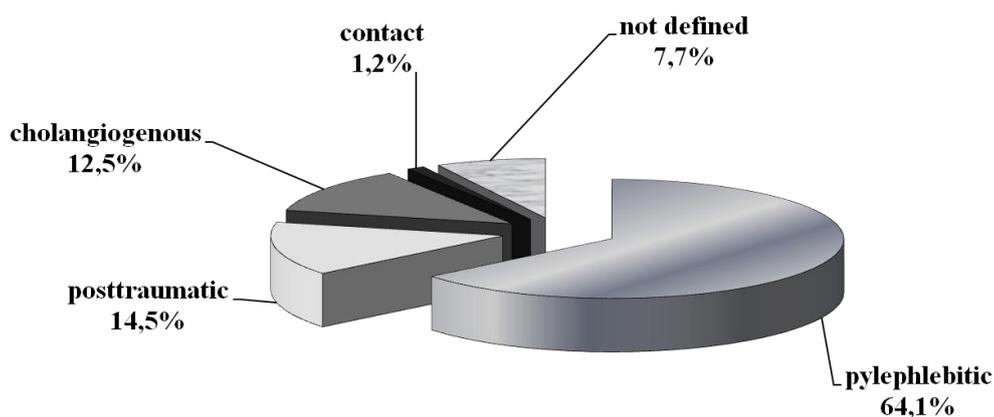


Fig. 1. The share of LA of various etiologies.

The cause of pylephlebitic AP in the majority of cases (120 (85.7% of the etiological subgroups)) — inflammatory diseases of the abdominal cavity (Table 1).

Table 1

Causes of the pylephlebitic AP

Disease	Number of patients	
	abs.	% of the etiological subgroup
chronic bacterial colitis	72	51.4
non-specific ulcerative colitis	18	12.9
Crohn’s disease	12	8.6
diverticulitis	10	7.1
appendicitis, appendiceal abscess	8	5.7
adnexitis	3	2.1
infected hemorrhoids	1	0.7
adrectal fistula	1	0.7
not defined	15	10.7
Total	140	100.0

In 15 cases, clinical and anamnestic analysis revealed no diseases that could have caused the development of pylephlebitic LA.

40 patients with pylephlebitic LA, including 10, in whom clinical and anamnestic analysis failed to reveal the cause of pylephlebitis, were examined to identify BOS after treatment. To compare, BOS tests were conducted in 36 patients with posttraumatic LA.

It was stated that 8 (20.0%) of 40 patients with pylephlebitic LA had BOS. In particular, BOS was detected in 7 of 10 patients with pylephlebitic LA of unknown origin, including 4 of 6 patients who reported long-term intake of proton pump inhibitors. Among patients with posttraumatic LA, BOS was detected only in 2 (5.6%) cases, which was significantly ($p < 0.05$) lower than upon pylephlebitic LA.

Messages, concerning that long-term use of proton pump inhibitors in medical history may provoke BOS, have been easily found in the profile literature in recent years [14, 15, 16], but the information about a possible association of these drugs and the risk of pylephlebitic LA is missing. The data obtained in this study on the higher

BOS frequency in patients with pylephlebitic LA as compared with posttraumatic abscesses allow hypothesize that BOS, in its turn, is a risk factor of pylephlebitic LA.

Thus, the literature data and the results of our own research allow to suggest that long-term use of proton pump inhibitors may potentiate the development of BOS, which increases the risk of pylephlebitic LA. This hypothesis requires further research, but at this stage you can (with a history of long-term use of proton pump inhibitors or verified BOS) recommend patients, who have clinical and laboratory signs of inflammation, an additional examination in order to identify a possible LA. Ultrasound is the best diagnostic method in this case from the point of information content, safety and availability.

Cholangiogenous LA were diagnosed in 31 patients. Reasons for their development are summarized in Table 2.

Table 2

Causes of cholangiogenous LA

Cause of cholangiogenous LA	Number of patients	
	abs.	% of the etiological subgroup
chronic cholangitis	9	29.0
long existing choledocholithiasis	7	22.6
tumour of the pancreatic head, complicated by obstructive jaundice	7	22.6
biliary and liver surgeries	3	9.7
acute cholecystitis	2	6.5
Caroli disease	1	3.2
chronic pancreatitis	1	3.2
primary sclerosing cholangitis	1	3.2

According to the analysis conducted, the main risk factors for cholangiogenous LA were: chronic cholangitis, long-existing choledocholithiasis and tumor of the pancreatic head, complicated by obstructive jaundice. The share of these factors had no statistically significant differences and totally amounted to 74.2%. The obtained data do not fully correspond to the opinion of some authors, indicating acute

pancreatitis as the leading present cause pylephlebitis and subsequent LA development.

Posttraumatic LA in the study group were found in 36 (44.5%) patients. In all cases, they had a clear history, namely — the presence of blunt trauma or injury of the abdomen.

The causes of post-traumatic LA were as follows. 17 (47.2% of the post-traumatic LA) patients had a concomitant injury of the chest and abdominal cavity with fractured ribs on the right (11 (30.6%) cases) and bilateral fracture (6 (16.7%) cases) in the medical history. In 9 (25.0%) cases, patients had a blunt abdominal trauma in the medical history, in 4 (11.1%) — concussion of the organs of abdominal cavity due to a drop or strike, 3 (8.3%) patients had abscess of residual cavity of area of the suturing liver parenchyma after a gunshot wound, in one case (for each) the cause of LA were: traumatic rupture of the right lobe of the liver hemangioma, gunshot and stabbed wounds of the liver.

Posttraumatic LA were characterized by prolonged and severe course due to the presence, in addition to the focus of suppuration, traumatic injuries of the surrounding tissues. All patients had "vague" clinical picture with the imposition of the symptoms caused by the traumas of other organs. In 6 (16.7%) cases traumatic LA were the sources of subdiaphragmatic or subhepatic abscesses in continuation, which also distorted the clinical picture.

Contact (secondary continuation) LA in the present study occurred in 2 patients on the background of destructive cholecystitis, in one — with renal abscess, and were in 2 (66.7%) patients with multiple and one — solitary.

Studying the medical history revealed that 88 (35.5%) of the patients of study group at the initial stage, when they contacted the health care institution, on the basis of clinical symptoms (weakness, loss of appetite, pain in the chest and the right side of the abdomen), laboratory data (leukocytosis, presence of stab shift typical for the inflammatory process) and chest x-ray results, were misdiagnosed. 56 (22.6%) of these patients (limitation of pleural sinus excursion) were wrongly diagnosed: acute respiratory viral infection — 20 (8.1%), pleurisy — 21 (8.5%), lobar pneumonia —

47 (18.9%) cases. Antibiotic therapy according to standard regimens was prescribed for patients empirically, in 42 (16.9%) cases attaining a temporary improvement, in 46 (18.6%) — without result. The lack of treatment effect was seen as a consequence of microflora resistance to the use of antibiotics, upon a deteriorating general condition of the patient build-up and laboratory signs of septic process 19 (7.7%) patients changed the antibiotic regimen. Antibiotics in some cases caused intestinal disorders because of acceding dysbiosis, which led to the further blurring of the clinical picture, distortion and vague symptoms, thus exacerbating the disease.

In terms of 12-15 days from the onset of the disease upon treatment failure, to find the septic source, patients had additional examinations — ultrasound in 70 (28.2%) cases, and CT of the chest and abdomen in 18 (7.2%) case. Examination revealed focal liver lesions, based on which 78 (31.5%) cases were diagnosed as LA, 10 (4.0%) — malignancy of the liver was suspected. Characteristically, LA in the presence of pleurisy in 20 of 21 patients was not accompanied by effusion into the abdominal cavity and subphrenic space on the right. Upon suspected malignancy of the liver, patients had further examinations, in particular, fine-needle biopsy under ultrasound guidance that allowed to define a correct diagnosis.

Thus, LA is the etiological heterogeneous group, in which the largest share belongs to pylephlebitic (61.4%), rarer detected posttraumatic (14.5%), cholangiogenous (12.5%), and single cases of contact abscesses (1.2 %).

In connection with a blurred or non-specific clinical picture, often severe condition of the patient, in some cases, the prevalence of symptoms of other diseases or damage of internal organs and bones, LA can't be promptly diagnosed in $35.5 \pm 3.0\%$ of patients. Therefore, if there are clinical and laboratory signs of inflammatory process, it seems necessary to conduct precision liver ultrasound to detect the possible LA. Lack of vigilance in relation to LA, which is often observed in the departments of therapeutic profile, leads to a prolongation of the diagnostics, misdiagnosis, inappropriate treatment, and, as a consequence, the worsening of the disease and poor health outcomes.

In connection with the above-said, we find it obligatory to conduct dynamic ultrasound of the abdomen, particularly the liver, upon clinical and laboratory signs of inflammatory processes (hyperthermia, weakness, leukocytosis) to identify LA echo-signs. The basis for the precise examination, including the assistance of other diagnostic techniques, with a view to identify potential LA, is the presence of risk factors. These risk factors, in particular, are: the presence of inflammatory diseases of the abdominal cavity, BOS, intake of proton pump inhibitors in the medical history (for pylephlebitic LA), diseases associated with cholestasis (for cholangiogenous LA), as well as surgeries and traumas in the medical history, and the presence of abscesses of another localization (respectively, for posttraumatic and contact LA).

In cases of serious condition, non-transportable patients, being in the profile department of the main disease (e.g., neurosurgery, polytrauma, etc.), in the absence of stationary ultrasound scanner in the department, ultrasound may be performed on the portable scanner, including air medical service, specialist arrival for consultation and conduction of therapeutic interventions.

Conclusions

1. Liver abscesses are etiologically inhomogeneous group, in which pylephlebitic (64.1%) abscesses had the biggest share, posttraumatic make up 14.5%, cholangiogenous — 12.5%, contact — 1.2%.
2. In the presence of clinical and laboratory signs of inflammatory processes (hyperthermia, weakness, leukocytosis), risk factors of the liver abscesses, it is recommended to carry out precision ultrasound of liver to detect possible ultrasound signs of abscess formation.
3. The risk factors of the liver abscesses are: the presence of inflammatory diseases of the abdominal cavity, bacterial overgrowth syndrome, diseases associated with cholestasis, surgeries and traumas in the medical history, presence of abscesses of another localization.

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It was found out that liver abscesses were etiologically inhomogeneous group, in which pylephlebitis (61.4%) abscesses had the biggest share, while posttraumatic (14.5%), cholangiogenous (12.5%) and single cases of contact (1.2%) abscesses were rarely detected. Because of the vague or non-specific clinical picture, severe patient's condition, prevalence of symptoms of other diseases or damage of the internal organs in some cases, liver abscesses cannot be timely diagnosed in $35.5\pm 3.0\%$ of patients. In the presence of clinical and laboratory signs of inflammatory processes (hyperthermia, weakness, leukocytosis), risk factors, in particular, bacterial overgrowth syndrome, inflammatory diseases of the abdominal cavity, receiving of proton pump inhibitors in anamnesis, diseases which are associated with cholestasis, operations and traumas in anamnesis, abscesses of other localizations, it is recommended to carry out precision ultrasound of liver to detect possible ultrasound signs of abscess formation.