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## Pyogenic liver abscess: literature review

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### Abstract

Pyogenic liver abscess (PLA) is one of the most common visceral abscesses. The main path of development is retrograde microorganism migration from the biliary tract. Other intra-abdominal infections, haematogenous dissemination or liver trauma can also be one of the reasons for the PLA formation. Nowadays these abscesses are more common between 60-70 years old patients. The main risk factors are diabetes mellitus, liver cirrhosis, biliary tract and pancreatic diseases. Usually abscesses are caused by polymicrobial gastrointestinal flora, which consists of aerobes and anaerobes. The main pathogens are *E. Coli* and *K. pneumoniae*. The most common symptoms of liver abscesses are fever and upper abdominal pain. Other symptoms may include chills, night sweats, malaise, nausea or vomiting, right shoulder pain, cough, dyspnoea, anorexia or recent unexplained weight loss. Laboratory tests are usually associated with an increase in liver enzymes such as aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP). Other significant laboratory tests may show hyperbilirubinemia or increase of international normalized ratio (INR). The main imaging test to confirm the diagnosis of liver abscess is ultrasonography (US). In order to determine a pyogenic liver abscess and causes of it, it is important to take blood culture and fine needle aspiration. Treatment of the PLA consists of antimicrobial therapy and drainage of the abscess. Cefuroxime and metronidazole or aminoglycoside cover gram-positive and gram-negative microorganisms and are the main antibiotics for PLA. Percutaneous needle aspiration (PNA) or percutaneous drainage (PCD) must be performed when abscesses are larger than 5 cm or patients did not improve clinically under antimicrobial therapy.

**Key words:** liver abscess, pyogenic, upper right quadrant abdominal pain, percutaneous drainage, percutaneous needle aspiration.

1.

## Introduction

Liver abscess is a puss filled mass inside the liver that can develop because of direct contact with infection of the biliary tract, liver injury or abscess leakage of other intra-abdominal infection via portal vein. It is a relatively rare, but a critical disease with 2-12% mortality if untreated [1-3]. Liver abscesses can be classified into three forms: pyogenic (usually caused by polymicrobial infection), amoebic (*Entamoeba Histolytica*) and fungal (most often *Candida* spp.). Pyogenic liver abscess (PLA) is the most common and accounts for 80% of all liver abscesses [4]. PLA can be distinguished by size and localization into large solitary abscesses localised in one liver lobe or small multiple abscesses localised throughout the parenchyma. Large abscesses cause subacute symptoms and must be drained, meanwhile small abscesses manifest by acute clinical symptoms and antimicrobial treatment is required first.

## 2. Epidemiology

Liver abscess is one of the most common visceral abscesses. The incidence of PLA is about 2,3 cases per 100,000 people. Several studies have found that PLA develops more often in men than in women [5-7]. In the past, PLA used to be more common between 40-50 years old people and the main cause was perforated appendicitis. In recent times, patients with PLA mean age has become 60-70 years whilst biliary system diseases are the leading cause [1, 4]. The most common risk factor is diabetes mellitus (DM), because hyperglycaemia weakens the immune system by altering neutrophil functions. Other risk factors include liver cirrhosis,

malignancy, immunosuppressive disorders, liver transplants and hepatobiliary or pancreatic diseases [2, 8].

## 3. Pathogenesis

Focal infection of the liver can be divided into several groups depending on the way the microorganisms entered the liver. Retrograde migration of microorganisms from the biliary tract to the liver parenchyma is the major source of PLA formation and accounts for about 60% of all ways [4]. Bile duct obstruction caused by gallstone or malignant obstruction leads to bile stasis, which is a great medium for the proliferation of bacteria [8]. Another common source is through the portal vein when microorganisms from another intra-abdominal infection enter the bloodstream, form emboli and travel to the liver. Also, PLA may be complicated by portal vein inflammation called pylephlebitis. Haematogenous dissemination from infection in the body such as infectious endocarditis or pyelonephritis also occurs as a possible source for PLA [1-3, 8]. About 3% of PAL are caused by liver trauma, which can either be penetrating and cause direct bacteria entry or be blunt and cause hemorrhage or necrosis which results in the formation of an abscess [1, 4]. In rare cases, foreign bodies, parasites, intrahepatic tumors or cysts can cause PLA [9-11].

## 4. Etiology

Most cases are polymicrobial; consist of aerobes and anaerobes. Gastrointestinal flora is the main source of microorganisms causing PLA. The most common pathogens are *E. Coli* and *K.*

pneumoniae [2, 4, 8]. Other gram-negative aerobes (*Pseudomonas* spp., *Proteus* spp., *Citrobacter* spp.) are more common in patients with biliary tract diseases [8]. Infection of *K. pneumoniae* is an increasing problem in Asia, where it is the main pathogen and accounts for about 80% cases of all PALs [12,13]. Furthermore, in most cases it occurs in patients with DM [8, 13]. The most common gram-positive aerobes are *S. milleri*, *Enterococcus* spp., *S. aureus*, *S. epidermidis* and *Streptococcus* spp. If *S. aureus* is identified as an isolated pathogen it is a sign to search for another source of infection in the body, which spreads hematogenously to the liver [1]. Anaerobic pathogens such as *Bacteroides* spp.,

*Fusobacterium* spp., *Actinomycetes* spp., *Clostridium perfringens* and anaerobic streptococcus usually occur as a combination with aerobic bacteria but can be found without it. The initial source for these microorganisms is pelvic abscess, appendicitis, diverticulitis and other gastrointestinal diseases [4, 8]. In patients with immunodeficiency fungal abscesses, especially caused by *Candida* spp. are common. Other important organisms are *Entamoeba histolytica*, which causes amoebic abscess, and parasite *Echinococcus granulosus*, which causes hydatid cyst. The frequency of most common pathogens compiled from the literature is shown in Table 1.

**Table 1.** Microbiologic etiology of PLA.

Pathogens	Frequency, %
<b>Gram-negative aerobes</b>	
<i>E. coli</i>	16 – 30
<i>K. pneumoniae</i>	5,6 – 16
<i>Pseudomonas</i> spp.	3,8 – 6,1
<i>Proteus</i> spp.	1,4 – 1,9
<i>Citrobacter</i> spp.	1,9
<b>Gram-positive aerobes</b>	
<i>S. milleri</i>	11 – 12,2
<i>Enterococcus</i> spp.	9,3 – 11,3
<i>S. aureus</i>	7,5 – 7,7
<i>Streptococci</i> spp.	1,1 – 13,2
<b>Anaerobic organisms</b>	
<i>Bacteroides</i> spp.	11,2 – 13,2
<i>Fusobacterium</i>	4,2
Anaerobic streptococci	6,1
<b>Fungi</b>	
<i>Candida albicans</i>	0,3 – 3,8
<i>Aspergillus</i> spp.	0,3

## 5.

### Symptoms

The most common symptoms of liver abscesses are fever and upper abdominal pain, with both presented in about 90% of the patients [14]. Other symptoms may include chills, night sweats, malaise, nausea or vomiting, right shoulder pain (due to phrenic nerve irritation), right upper quadrant pain, cough, dyspnoea, anorexia or recent unexplained weight loss. Also, sometimes patients could describe a presence of dark urine or clay-coloured stools [15]. If the abscess ruptures (a rare complication) then patients may present in distress or even septic or anaphylactic shock [1].

The most common findings during physical examination in patients with liver abscesses is hepatomegaly and right upper quadrant tenderness. It has been noticed that jaundice is also a common finding if abscess is pyogenic origin [16]. Splenomegaly or ascites is an unusual sign of liver abscess and both are only present in advanced stages of the illness [17]. If abscess is caused by *Klebsiella*, it also may send septic emboli to the eye, meninges, and brain. Symptoms of these systems may last even after liver abscess treatment [1].

## 6. Diagnostics

Enzymes describing liver function like aspartate aminotransferase (AST) and alanine aminotransferase (ALT) may increase in about half of the patients with liver abscess, while alkaline phosphatase may be present in more than 80% of the cases. AST and ALT may evaluate higher if the process is acute. Hyperbilirubinemia

is present in only a small proportion of patients (30%), while lower serum albumin levels, and increase of international normalized ratio (INR) are observed in about 80% of the patients [18]. It was also observed that the value of these indicators may depend on the size of the abscess. For example, INR, alkaline phosphatase, and liver enzymes (ALT, AST) increase, and serum albumin decreases with the size of the abscess [19]. While these tests may not have real value in differentiating pyogenic liver abscess from others, it may give us preliminary opinion about the size of the abscess and effect of the treatment. To determine a pyogenic liver abscess and causes of it, it is important to take blood culture and fine needle aspiration under ultrasonography (US) or computed tomography (CT) guidance. Blood or aspirate culture are positive only in 50% and 40% of the cases, respectively. Despite not that high accuracy, these tests can provide useful information prior to antimicrobial treatment [20].

The main imaging test to confirm the diagnosis of liver abscess is ultrasonography (US). US sensitivity in the diagnosis of liver abscesses is about 85%. It may also depend on the location of the abscess. Sensitivity may increase if abscess is localized in 4th or 5th liver segments. But location in segment 8 is mostly associated with delayed diagnosis by US [21]. The pathological visual aspect of abscess is hyper or hypoechoic lesions with occasional debris or septation [1]. When ultrasound is not informative enough, we should use additional instrumental examinations. Some studies have shown that about 50% of the patients with liver abscesses needed a computed tomography and 3% of the

patients needed a magnetic resonance imaging to confirm the diagnosis [7].

Computed tomography is not the first-line test for diagnosing liver abscesses, but it has sensitivity of 95-100% [22]. If possible, it is better if CT scan is done with intravenous contrast. There are several signs common with liver abscesses. The „Double target sign“ is described as a well-defined, round lesion with central hypoattenuation. The inner layer represents the pyogenic membrane, and the outer layer is due to edema of the hepatic parenchyma [23, 24]. Peripheral rim enhancement or surrounding edema are not common findings but are specific for liver abscess [ 2]. The “cluster sign” may also be present and occurs when multiple low-attenuation lesions aggregate in a localized area to form a solitary larger abscess cavity.

Magnetic resonance imaging (MRI) is also a sensitive imaging test for detection of liver abscess, but it is less rapidly available. On MRI, abscesses often appear to have central low signal intensity on T1-weighted imaging and high signal intensity on T2-weighted imaging [23,24].

## 7. Treatment

The treatment of PLAs depends on the stage of the disease and the size of abscess. Empirical antimicrobial therapy should be started at the onset of clinical sign of the infection. Antibiotics should cover the most common pathogens such as gram-positive coccus and gram-negative bacilli [25, 20]. The most used combination is intravenous cefuroxime and metronidazole or aminoglycoside. Antibiotics can be subsequently adjusted according to the

susceptibility of the microorganisms. The duration of antibiotics treatment usually lasts from 21 to 35 days, parenteral therapy is recommended for the first 14 days and can be changed to oral if there is a favorable clinical response. [20, 27]. Antimicrobial therapy alone is enough treatment for smaller than 5cm abscess or small multiple abscesses in about 80-90% of cases [25, 26]. In patients with hepatic abscess due to bile duct infection, biliary hypertension should be eradicated ensuring bile drainage [1]. This is usually done during endoscopic retrograde cholangiopancreatography, but sometimes percutaneous bile duct drainage or even open surgery is required. US or CT guided percutaneous needle aspiration (PNA) or percutaneous drainage (PCD) is used for larger than 5cm abscesses or smaller abscesses which did not improve clinically [28]. PNA is performed by a 17-27 Gauge needle. Once the needle tip is within the abscess cavity the pus is aspirated and then the needle is removed [29]. During PCD, a 6-10 French pig-tail catheter is used. It is placed via the Seldinger or trocar techniques [22]. Then a catheter is secured to a skin for continuous external drainage. The removal of the percutaneous drain is based on the patient's clinical and laboratory response. The median duration of drainage may vary from 12.6  $\pm$  14 days, and catheter is often removed when daily output is less than 10 ml/day [22,26]. Both PNA and PCD are safe methods of draining liver abscesses. However, several studies have shown that PCD (100%) is more effective than PA (67 %) in the management of liver abscess [29 - 31]. Surgical interventions are rare, but should be considered in patients with large, complex, or multiple abscesses, underlying disease, or with

those who have failed percutaneous drainage [32].

## 8. Prognosis

The current mortality rate in people with PLA is low, ranging from 0,5 - 4%, because of new drainage methods and antibiotics effectiveness for specific microorganisms [33 - 35]. Older age, immunosuppressive condition, delayed treatment and complications, like rupture of the abscess and peritonitis are associated with a higher mortality rate of 12% [36].

## 9. Conclusion

There are lots of causes of the PLA, but the main remains to be infection of the biliary tract. Despite usual gastrointestinal flora, *K. pneumoniae* is getting more common, especially in Asia. US is considered as the gold standard for diagnosing PLA. Best results in PLA management and treatment are reached using antimicrobial therapy and percutaneous drainage of the abscess together. However, for older, immunosuppressed patients or if treatment is delayed, causing complications such as peritonitis, mortality rate is higher and counts up to 12%.

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