Pyogenic Liver Abscess

Sarah Longworth M.D.* and Jennifer Han M.D., M.S.C.E*,†,‡

Pyogenic liver abscess (PLA) is a rare disease. Although once uniformly fatal, advances in imaging modalities and antimicrobial therapy have led to significant improvements in outcomes.

Epidemiology

The disease was first described by Hippocrates around 400 BC, but the seminal review of PLA was published by Ochsner and colleagues in 1938. Forty-seven cases were described, largely occurring in young men with appendicitis, with significant reductions in mortality seen with surgical treatment.¹

PLA is a rare condition with significant geographic variation, with a reported annual incidence of 3.6 cases per 100,000 individuals in the United States,² but up to 17.6 per 100,000 in Taiwan.³ There is a slight predominance in males. Due to changes in etiology, PLA now primarily affects older individuals, with peak incidence between 50 to 60 years of age.

Risk factors include diabetes mellitus,⁴ underlying hepatobiliary or pancreatic disease, and gastrointestinal malignancy.^{5,6} In up to 15% of cases, PLA is the initial manifestation of an occult intra-abdominal malignancy.⁷

Pathogenesis: Etiology and Microbiology

Biliary tract disease, including chole(doch)lithiasis, obstructing tumors, strictures, and congenital biliary tree anomalies, has replaced appendicitis as the most common identifiable cause of PLA.^{5,8} Portal vein seeding in the setting of bowel and/or pelvic pathology (eg, appendicitis, diverticulitis) is the second most common etiology.^{5,6,9} Hepatic artery seeding from hepatic artery thrombosis and bacteremia accounts for an increasing number of cases of PLA, largely as a result of

increased use of immunosuppressants and hepatic artery chemoembolization.⁵ Less commonly, PLA develops via direct extension of infection from the gallbladder, subphrenic or perinephric spaces, or following penetrating trauma. A reported 18%-66% of PLA are cryptogenic, with no underlying cause identified^{6,9-11} (Table 1).

The microbiology of PLA varies by etiology and geography. Most PLA cases are polymicrobial, with commonly identified pathogens including mixed enteric facultative and anaerobic species. In Western series, the most commonly isolated organism is *Escherichia coli*,^{9,12,13} followed by *Klebsiella pneumoniae*, *Enterococcus*, and *Streptococcus* species. *Staphylococcus aureus* and other skin flora are typically isolated in instances of penetrating trauma and following hepatic chemoembolization.¹⁴

First described in the 1980s in Taiwan, the K1 and K2 serotypes of *K. pneumoniae* have emerged as the most common causes of PLA in much of Asia.^{10,15,16} Recent studies suggest that the incidence of this pathogen may also be increasing in the Western hemisphere.^{8,17} These strains demonstrate a hypermucoviscous phenotype due to increased extracapsular polysaccharide production, with increased resistance to phagocytosis and serum complement killing (Fig. 1). These cases are generally cryptogenic in origin, and associated with high rates of complications, including bacteremia (48%-72%) and metastatic infection (10%-45%), most commonly endophthalmitis.^{18,19}

Clinical Presentation and Diagnosis

The clinical presentation of PLA is nonspecific; thus, a high index of suspicion is required for timely diagnosis. The classic triad of right upper quadrant abdominal pain,

Abbreviations: CT, computed tomography; PLA, pyogenic liver abscess.

From the *Division of Infectious Disease, Hospital of University of Pennsylvania, Philadelphia, PA, †Department of Biostatistics and Epidemiology, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, ‡Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA.

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TABLE 1 Etiology of PLA

Biliary source
• Chole(dochol)lithiasis
• Obstructing tumor
• Stricture
• Congenital anomaly of biliary tree
Portal vein seeding, bowel and/or pelvic pathology
• Appendicitis
• Diverticulitis
• Inflammatory bowel disease
• Postoperative infection
Hepatic artery seeding, hematogenous infection
• Hepatic artery thrombosis/chemoembolization
• Bacteremia
Direct extension
• Subphrenic abscess
• Perinephric abscess
• Cholecystitis
Penetrating trauma
Cryptogenic

fevers/chills, and malaise is only present in approximately 30% of patients. Other symptoms include rigors, nausea/vomiting, anorexia, weight loss, and generalized weakness. Less commonly, patients may present with cough, hiccups, or referred right shoulder pain due to diaphragmatic irritation. Common physical examination findings include right upper quadrant abdominal tenderness, jaundice, and hepatomegaly.

Laboratory evaluation often reveals leukocytosis, normocytic anemia, hypoalbuminemia, and prolonged prothrombin time. Elevated inflammatory markers, including erythrocyte sedimentation rate and C-reactive protein, are sensitive, but nonspecific for diagnosis. An elevated alkaline phosphatase is

Figure 1 Hypermucoviscous phenotype of K1/K2 serotypes of *Klebsiella pneumoniae*. The K1/K2 serotypes of *K. pneumoniae* demonstrate a mucoid appearance on culture plates and also exhibit a positive string sign, reflective of their increased extracapsular polysaccharide production.²⁷ [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Figure 2 Ultrasound appearance of PLA. A 33-year-old male with type 1 diabetes who presented with septic shock was found to have an 11 cm × 11 cm × 12 cm hepatic abscess in right hepatic lobe, initially managed with percutaneous drainage, but ultimately requiring partial hepatectomy. Note the large multilobulated hypoechoic lesion on ultrasound.

the most commonly observed laboratory abnormality, occurring in up to 90% of patients. Approximately 50%-65% of patients will have elevated aspartate and alanine aminotransferases and total bilirubin levels.^{6,11,20} Blood cultures are positive in 30%-60% of cases, although rates are higher with *K. pneumoniae*. Organisms are isolated from the majority (70%-80%) of abscess aspirates.^{5,10}

Computed tomography (CT) and ultrasound are the preferred imaging modalities for diagnosis of PLA, the former being slightly more sensitive (93%-97% versus 83%-95%).^{20,21} These studies may also be of utility in identifying the underlying etiology. PLAs appear as hypo- or hyperechoic lesions with internal debris on ultrasound, and non-enhancing hypodense lesions with rim enhancement on CT (Figs. 2 and 3). PLA presents as a solitary abscess in 65%-85% of cases, with a predilection for the right hepatic lobe⁸⁻¹¹ due in part to its receipt of the majority of portal venous return.

Treatment

Management of PLA has dramatically evolved over the past three decades due to advances in diagnostic and interventional radiology. Percutaneous drainage, along with targeted antimicrobial therapy, is the mainstay of therapy. Criteria for percutaneous drainage include abscess size >5 cm,²² ongoing pyrexia despite 48 to 72 hours of appropriate medical therapy, and clinical or imaging features concerning for impending perforation.²³ Percutaneous drainage via ultrasound or CT with placement of a drainage catheter is associated with high rates of

Figure 3 Computed tomography (CT) appearance of PLA. A 52-year-old female with colorectal cancer, status post biliary stenting for presumed malignant obstruction, admitted with nausea, vomiting, and fever, was found to have *E. coli* bacteremia and a large multiseptated hypodense lesion with peripheral rim enhancement on CT, typical of a PLA.

success.^{24,25} However, 8%-36% of patients will fail this approach and require surgery.^{13,26}

Indications for surgical drainage include abscess rupture, uncorrected primary pathology, incomplete percutaneous drainage, inadequate clinical response after 4–7 days of percutaneous drainage, and multiloculated abscesses.^{6,13}

No randomized controlled trials have been performed to evaluate empiric antimicrobial regimens or optimal durations of therapy. Empiric regimens should be formulated

based on suspected etiology and local antibiotic susceptibility patterns, and modified based on culture results. Recommendations include parenteral therapy for 2–3 weeks or until there is a favorable clinical response, followed by an oral regimen for 2–6 weeks or until clinical, laboratory, and radiographic studies demonstrate abscess resolution.

Outcomes

Prior to 1980, the overall mortality rate associated with PLA was greater than 50%. However, improvements in diagnostic and therapeutic radiology, coupled with advances in microbiological identification and therapy, have led to dramatic reductions in mortality. Case series from the past decade report mortality rates of 2%-14%.^{8–11} Risk factors for mortality include advanced age, malignancy, shock, jaundice, multiple abscesses, hemoglobin <10 g/dL, and elevated blood urea nitrogen.^{5,13}

Conclusion

PLA remains a rare disease, the etiology and microbiology of which have significantly evolved over time. Percutaneous drainage, combined with directed antibiotics, has become the mainstay of therapy. Improvements in diagnostic and therapeutic modalities have led to tremendous decreases in mortality in recent years.

CORRESPONDENCE

Sarah Longworth, Hospital of University of Pennsylvania, Division of Infectious Disease, Philadelphia, Pennsylvania, United State
E-mail: sarah.longworth@uphs.upenn.edu

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