Pyogenic liver abscess

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INTRODUCTION

Pyogenic liver abscesses usually develops in the context of biliary disease, portal pyemia of various causes, through arterial hematogenous seeding, or via direct spread.

The clinical approach to pyogenic liver abscess will be reviewed here. Amebic abscesses and pyogenic abscesses caused by *Klebsiella pneumoniae* are discussed separately. (See "Extraintestinal Entamoeba histolytica amebiasis" and "Invasive liver abscess syndrome caused by Klebsiella pneumoniae".)

EPIDEMIOLOGY

Prevalence — Liver abscesses are the most common type of visceral abscess (an abscess within an intra-abdominal organ). In a report of 540 cases of intra-abdominal abscesses that also included intra- and retro-peritoneal abscesses, pyogenic liver abscesses accounted for 48 percent of visceral abscesses and 13 percent of intra-abdominal abscesses overall [1]. The annual incidence of liver abscess has been estimated at 2.3 cases per 100,000 people and is higher among men than women (3.3 versus 1.3 per 100,000) [2-4]; substantially higher rates have been reported in East Asian countries (up to 17.6 cases per 100,000) [5,6].

Risk factors — Risk factors include diabetes mellitus, underlying hepatobiliary or pancreatic disease, liver transplant, and regular use of proton-pump inhibitors [2,3,7-9]. Geographic and host factors may also play a role; for example, a primary invasive liver abscess syndrome due to

K. pneumoniae has been described in East Asia. As mentioned, this is discussed separately. (See "Invasive liver abscess syndrome caused by Klebsiella pneumoniae".)

Patients with chronic granulomatous disease (CGD), a rare genetic disorder characterized by recurrent infections, are also at risk for liver abscess. (See "Chronic granulomatous disease: Pathogenesis, clinical manifestations, and diagnosis", section on 'Infections'.)

Association with colorectal neoplasia — *K. pneumoniae* is the primary cause of pyogenic liver abscesses in several parts of Asia, and studies from these regions have suggested an association with underlying colorectal cancer [10-16]. It is unclear whether these findings can be applied to other parts of the world.

In a large retrospective analysis of claims data from the universal insurance program in Taiwan, the incidence of any subsequent gastrointestinal malignancy diagnosis among 14,690 patients who had been diagnosed with pyogenic liver abscess was fourfold higher than that among 58,760 controls matched for age, sex, and underlying diabetes mellitus (10.8 versus 2.5 cases per 1000 person-years) [15]. Colorectal carcinoma was the most common malignancy in both cohorts but was more frequent among liver abscess patients (7.3 versus 1.6 cases per 1000 person-years). In a separate retrospective study from Taiwan, in which 1257 patients with pyogenic liver abscess were observed to have a high risk of subsequent liver or colorectal carcinoma, the greatest excess risk of a cancer diagnosis was in the first three months after the abscess diagnosis [11]. In one systematic review of 12 studies, the pooled prevalence rate of colorectal cancer among over 18,000 patients with pyogenic liver abscess (mainly caused by *K. pneumoniae*) was 8 percent (compared with 1.2 percent in controls) [16].

In most studies that evaluated causative pathogens, liver abscesses caused by *K. pneumoniae* appear to have a stronger association with colorectal cancer than those caused by other organisms [12-14], probably because most other organisms seeded the liver from biliary tract diseases. The long-term follow-up prevalence of colorectal cancer among pyogenic liver abscess patients remained 2.3 to 3.2 percent [10,14]. Despite the limitations of these retrospective studies, the findings suggest that clinicians should consider the possibility of an occult colorectal neoplasia in patients diagnosed with pyogenic liver abscess, particularly due to *K. pneumoniae* and in the absence of apparent underlying hepatobiliary disease.

PATHOGENESIS

A considerable proportion of pyogenic liver abscesses follow one or more episodes of portal vein pyemia, often related to bowel leakage and peritonitis. Another important route is direct

spread from biliary infection. Underlying biliary tract disease, such as gallstones or malignant obstruction, is present in 40 to 60 percent of cases [2,17,18]. Occasionally, abscesses arise from surgical or penetrating wounds, including injury from migration of an ingested foreign body [19,20].

Liver abscesses may also result from hematogenous seeding from the systemic circulation. A monomicrobial liver abscess due to a streptococcal or staphylococcal species should prompt evaluation for an additional source of infection, including infectious endocarditis.

MICROBIOLOGY

Many pathogens have been described; this variability reflects the different causes, types of medical intervention (such as biliary tree stenting, or immunosuppression due to cancer chemotherapy) and geographic differences. Most pyogenic liver abscesses are polymicrobial; mixed enteric facultative and anaerobic species are the most common pathogens. Anaerobes are probably under-reported because they are difficult to culture and characterize in the laboratory. For example, in one series of 233 cases, mixed facultative and anaerobic species were implicated in one-third of patients, and bacteremia was documented in 56 percent of cases [2].

The highly variable microbiology justifies pursuing a microbiological diagnosis in virtually every case. Potential pathogens include the following:

- Enteric gram-negative bacilli, particularly *Escherichia coli* and *K. pneumoniae*, are the most commonly identified pathogens [21]. In East Asia, *K. pneumoniae* is an important cause of primary liver abscess. (see "Invasive liver abscess syndrome caused by Klebsiella pneumoniae").

- Streptococci were the most common pathogen in one series of pyogenic liver abscess in the United States [22]. In particular, the *Streptococcus milleri* group (including *Streptococcus anginosus*, *Streptococcus constellatus*, and *Streptococcus intermedius*) is an important cause of liver abscess. When implicated, it should prompt a search for simultaneous metastatic infections at other locations. (See "Infections due to the *Streptococcus anginosus* (*Streptococcus milleri*) group".)

- *Staphylococcus aureus*, *Streptococcus pyogenes*, and other gram-positive cocci are recognized pathogens in specific circumstances. As an example, streptococcal and staphylococcal species were the most common pathogens in a population-based analysis of pyogenic liver abscess in children, among whom liver transplantation was a major risk

factor [23]. In a report of liver abscesses in patients who underwent transarterial embolization for hepatocellular carcinoma, gram-positive cocci accounted for 60 percent of pathogens [24].

Candida coinfection along with typical bacteria has also been described [22].

CLINICAL MANIFESTATIONS

Typical features — The typical clinical manifestations of pyogenic liver abscess are fever and abdominal pain. Other common symptoms include nausea, vomiting, anorexia, weight loss, and malaise.

Fever occurs in approximately 90 percent of patients, and abdominal symptoms occur in 50 to 75 percent [2,3,17,25]. Abdominal symptoms and signs are usually localized to the right upper quadrant and may include pain, guarding, the rocking sign (pain caused by gently rocking the patient's abdomen), and even rebound tenderness. Approximately one-half of patients with liver abscess have hepatomegaly, right upper quadrant tenderness, or jaundice [25]. The absence of right upper quadrant findings does not exclude liver abscess.

Laboratory abnormalities often include elevated bilirubin and/or liver enzymes. Serum alkaline phosphatase is elevated in 67 to 90 percent of cases, and serum bilirubin and aspartate aminotransferase concentrations are elevated in approximately one-half [2,17,25].

Other laboratory abnormalities may include leukocytosis, hypoalbuminemia, and anemia (normochromic, normocytic).

On chest imaging, an elevated right hemi-diaphragm, right basilar infiltrate, or right-sided pleural effusion can be seen in 25 to 35 percent of cases [26]. Typical findings on liver imaging are discussed elsewhere. (See 'Imaging' below.)

Complications — Abscess rupture is a rare complication, occurring in 3.8 percent of 602 patients in one series from Korea [27]. Abscess diameter >6 cm and coexisting cirrhosis are the main risk factors for rupture, with most ruptures being perihepatic or into the pleural space. It is expected that rupture and other dramatic complications are more likely to occur in remote and low-resource settings or other situations where there is limited access to diagnostic imaging and therapeutic interventions [28].

DIAGNOSIS

Overview — The finding of one or more space-occupying liver lesions identified on abdominal imaging raises the possibility of pyogenic liver abscess. Features that should prompt liver imaging include fever, especially with one or more of the following: right upper quadrant pain, elevated liver enzymes, or hyperbilirubinemia (see "Evaluation of the adult with abdominal pain", section on 'Right upper quadrant pain'). However, the clinical symptoms of liver abscess can be both subtle and protean; abdominal imaging is an appropriate approach to evaluate for persistent fever without alternative explanation, even in the absence of right upper quadrant signs or symptoms.

Certain imaging features favor the diagnosis of liver abscess over other lesions, such as cysts or tumors (see 'Imaging' below). When findings point to one or more liver abscesses, this should prompt diagnostic aspiration or drainage as soon as possible. This can also be potentially therapeutic. Blood cultures should also be obtained. (See 'Obtaining an abscess specimen' below.)

If the patient is critically ill with sepsis, organ dysfunction, or septic shock, then empiric antibiotic therapy should be commenced as soon as blood cultures have been collected and prior to abscess aspiration. If the patient does not have sepsis and the aspiration can be done within several hours, then empiric antibiotic therapy should be withheld until immediately following aspiration to increase the chances of a microbiologic diagnosis that will guide subsequent treatment. (See 'Antibiotic therapy' below and "Sepsis syndromes in adults: Epidemiology, definitions, clinical presentation, diagnosis, and prognosis", section on 'Sepsis'.)

When a patient with a liver lesion on imaging that is purulent on aspiration and/or has pathogens identified on Gram stain or culture of the aspirate material or in blood, the diagnosis of liver abscess is confirmed. If bacterial pathogens are not identified on microbiologic evaluation, clinicians should consider the possibility of "atypical" pathogens. (See 'Differential diagnosis' below.)

If a streptococcal or staphylococcal species is recovered as a single pathogen from a liver abscess, this should prompt evaluation for a hematogenous source of infection, in particular infectious endocarditis. (See "Clinical manifestations and evaluation of adults with suspected left-sided native valve endocarditis".)

Laboratory testing — Blood cultures are essential. They are positive in up to 50 percent of cases [2,29]. If possible, at least two sets of both aerobic and anaerobic cultures should be obtained, ideally before the administration of empiric antibiotic therapy.

We routinely check serology for *E. histolytica* on initial diagnosis in patients who do not have an evident predisposition to pyogenic abscess, such as recent biliary or abdominal surgery, known

biliary disease, or prior biliary instrumentation. Most clinicians are aware of the known risks for amebic liver abscess that include living or travelling through high-incidence regions, but amebic liver abscesses can occur in any region of the world [30]. (See "Extraintestinal Entamoeba histolytica amebiasis", section on 'Amebic liver abscess'.)

If not already done, we recommend additional laboratory studies including complete blood count, electrolytes, blood urea nitrogen and creatinine, liver enzymes, and bilirubin levels.

Imaging — Ultrasound and computed tomography (CT) are the first choice imaging studies for identification of liver abscess [19]. CT is slightly more sensitive than ultrasound (approximately 95 versus 85 percent) [31,32]. But ultrasound is often more immediately available, especially in low-resource settings. If ultrasound does not demonstrate any abnormality, then CT may provide the diagnosis when suspicion of liver abscess remains high. Imaging can also identify other intra-abdominal abnormalities that indicate a potential predisposing condition, such as biliary tree disease or thrombosis of the portal vein (which could suggest pylephlebitis) [33]. (See "Pylephlebitis".)

- **Ultrasound** – On ultrasound, pyogenic abscesses can range from hypoechoic to hyperechoic lesions [34,35]. Ultrasound may also show internal echoes reflecting debris or septation.

- **CT scan** – If a CT scan is done, it should ideally be with intravenous contrast. The most typical finding is a well-defined, round lesion with central hypoattenuation [34,35]. However, abscesses can also be more complex with loculated subcollections or an irregular border (image 1 and image 2). Peripheral rim enhancement or surrounding edema are not common findings but are relatively specific for liver abscess.

  Although a study from Taiwan suggested that thin walls, lack of rim enhancement, metastatic infection, and lack of biliary disease on CT imaging were associated with *K. pneumoniae* compared with other pathogens, it is unclear if these are discriminating features in other regions, where the incidence of *K. pneumoniae* liver abscess is lower [36]. Microbiologic studies remain the only way to definitively determine the bacterial cause of a pyogenic liver abscess.

Liver abscesses most commonly involve the right lobe of the liver, probably because it is larger and has greater blood supply than the other lobes. Abscesses need to be distinguished from tumors and cysts. Cysts appear as fluid collections without surrounding stranding or hyperemia. Tumors have a solid radiographic appearance and may contain areas of calcification. Necrosis and bleeding within a tumor may lead to a fluid-filled appearance; in such circumstances, radiographic differentiation from abscess can be challenging.

Imaging studies cannot reliably distinguish pyogenic liver abscess from amebic abscess [37]. (See "Extraintestinal Entamoeba histolytica amebiasis", section on 'Amebic liver abscess'.)

Other imaging modalities are less commonly used for diagnosing pyogenic liver abscess. While magnetic resonance imaging (MRI) is sensitive, it is not widely available outside well-resourced health services [38]. On MRI, abscesses often appear to have central low signal intensity on T1-weighted imaging and high signal intensity on T2-weighted imaging [34].

Radiolabeled white blood cell scans are less useful for distinguishing abscess from other causes of liver mass.

Obtaining an abscess specimen — We attempt CT or ultrasound-guided drainage of all suspected liver abscesses to confirm the diagnosis and identify the bacterial pathogens. In cases of small single abscesses, needle aspiration may be sufficient for therapeutic drainage; in most other cases, a drainage catheter is warranted. (See 'Drainage' below.)

The character of the aspirate should be noted; purulent material is expected for pyogenic liver abscesses. If macroscopically purulent material is not obtained, the possibility of alternative diagnoses should be considered while continuing empiric antibiotic therapy. In such cases, the aspirate or biopsy material should be submitted for histopathology and/or cytology in addition to microbiology.

All aspirate material should be sent for Gram stain and culture (both aerobic and anaerobic). Anaerobic culture should be specifically requested on the laboratory requisition because special handling is required. Some of the abscess material should be saved in the laboratory for further testing in case routine Gram stain and culture do not identify a bacterial pathogen. Such testing could include microscopy and culture for fungi and mycobacteria, antigen or polymerase chain reaction (PCR) testing for *E. histolytica*, special stains for parasites, and 16S rRNA PCR testing for fastidious bacteria.

Cultures obtained from existing percutaneous drains are **not** sufficiently reliable for guiding antimicrobial therapy, since they are often contaminated with skin flora and environmental organisms. This was demonstrated in a study of 66 cases of liver abscess; culture results obtained via radiographic guidance were compared with culture results obtained from a drain that had been in place for at least 48 hours [39]. Cultures from percutaneous specimens correlated with cultures from drainage catheters in only one-half of cases. Treatment based upon drainage culture results alone would have led to inappropriate therapy for the remaining patients.

DIFFERENTIAL DIAGNOSIS

Pyogenic liver abscess often presents with fever, right upper quadrant pain and tenderness, and elevated liver enzymes. Other potential diagnoses with similar signs and symptoms include acute hepatitis of any cause (eg, viral, drug induced, alcoholic), primary or secondary liver tumors, right lower lobe pneumonia, acute cholangitis, and acute cholecystitis. Timely liver imaging can help differentiate liver abscess from these other diagnoses. (See "Causes of abdominal pain in adults", section on 'Right upper quadrant pain'.)

The primary differential diagnosis for an apparent liver abscess on imaging studies is an amebic liver abscess, caused by *E. histolytica*. Amebic liver abscesses can occur anywhere in the world and have been reported in Australia, the United States, and Europe in patients without any travel history [40-42]. The clinical course and imaging appearance may be difficult to distinguish from pyogenic liver abscess. Amebic abscess is best distinguished from pyogenic liver abscess by *E. histolytica* serology. This is discussed in detail separately. (See "Extraintestinal Entamoeba histolytica amebiasis", section on 'Amebic liver abscess'.)

Other pathogens less commonly cause liver lesions, and are managed differently than pyogenic liver abscesses. These include:

- *Mycobacterium tuberculosis* – Tuberculous liver abscesses are uncommon, and when they do occur usually manifest as multiple small abscesses (miliary tuberculosis). Nevertheless, the possibility should be considered in patients at risk for prior exposure when typical pyogenic organisms are not recovered from liver aspirate cultures [37,39]. (See "Clinical manifestations, diagnosis, and treatment of miliary tuberculosis".)

- *Burkholderia pseudomallei* – This is the agent of melioidosis and can be identified by growth on culture of the abscess aspirate. Endemic areas include Southeast Asia, Northern Australia, South Asia (including India), and China. (See "Melioidosis: Epidemiology, clinical manifestations, and diagnosis".)

- *Echinococcus* species – Hepatic hydatid cysts are also space-occupying lesions in the liver but usually have a distinct appearance on imaging. Serology is the key to diagnosis. (See "Echinococcosis: Clinical manifestations and diagnosis".)

- *Candida* species – Hepatosplenic candidiasis usually manifests as microabscesses throughout the liver parenchyma. It can occur in patients with hematologic malignancies during recovery of neutrophil counts following a neutropenic episode. *Candida* liver abscesses more resembling pyogenic liver abscesses have also been described, even in

immunocompetent patients. They should be identified on microscopy and/or growth from abscess cultures [43-45]. *Candida* can also be a copathogen with other organisms more typical for pyogenic liver abscesses [22]. (See "Chronic disseminated candidiasis (hepatosplenic candidiasis)".)

- Other uncommon infectious causes of multiple liver lesions include *Bartonella*, *Fasciola*, and endemic fungal infections. These lesions are usually small and nodular. (See "Microbiology, epidemiology, clinical manifestations, and diagnosis of cat scratch disease", section on 'Visceral organ involvement' and "Bartonella infections in people with HIV", section on 'Bacillary peliosis hepatis and splenitis' and "Liver flukes: Fascioliasis", section on 'Imaging' and "Pathogenesis and clinical manifestations of disseminated histoplasmosis", section on 'Pathology'.)

Noninfectious etiologies that can have a radiographic appearance similar to a pyogenic liver abscess include a simple cyst, a necrotic tumor, and a biloma (collection of bile). These can be distinguished by the gross and/or pathologic examination of the liver lesion aspirate.

TREATMENT

The principle elements of treatment are drainage and antibiotic therapy.

Drainage — We strongly recommend drainage whenever practical and feasible; it is both diagnostic and therapeutic (see 'Obtaining an abscess specimen' above). Percutaneous drainage should be CT or ultrasound-guided. Simple aspiration may be sufficient for some small abscesses but, where possible, placement of a drainage catheter is preferred [46,47]. Two large randomized controlled trials from India have shown that, for pyogenic liver abscesses >5 cm in diameter, percutaneous catheter drainage reduces time to recovery and shortens hospital stay when compared with percutaneous aspiration alone. Other options include open surgical drainage, laparoscopic drainage, or drainage by endoscopic retrograde cholangiopancreatography (ERCP). Drainage by ERCP can be useful for liver abscesses in patients with previous biliary procedures whose infection communicates with the biliary tree [18,48]. Endoscopic ultrasound-guided drainage is an emerging technique that appears to be safe and effective for difficult-to-access liver abscesses [49,50].

Surgical drainage (either open or laparoscopic) is appropriate when there is an underlying process that warrants surgical management. Otherwise, the approach to abscess drainage depends on the size and number of abscesses.

- **Single, unilocular abscesses with a diameter ≤5 cm** – Percutaneous drainage with either catheter placement or needle aspiration only is acceptable, as both result in successful outcomes with smaller abscesses [51-54]. The choice between the two depends on local availability; catheter placement is preferred. If only needle aspiration is available, repeated aspiration may be required in up to half of cases [51,52]. If inserted, drainage catheters should remain in place until drainage is minimal (usually up to seven days). Some abscesses may be too small to drain; this is a technical decision of the clinician conducting the procedure.

- **Single, unilocular abscesses with diameter >5 cm** – We also suggest percutaneous drainage for unilocular abscesses larger than 5 cm and prefer drainage with placement of a catheter rather than needle aspiration alone. As above, drainage catheters should remain in place until drainage is minimal (usually up to seven days).

  Catheter drainage for larger abscesses is supported by results of a meta-analysis of five randomized trials comparing catheter drainage with needle aspiration in over 300 patients with pyogenic liver abscess, most of which were larger than 5 cm [55], as well as two subsequently published randomized controlled trials [46,47]. Catheter drainage resulted in a higher success rate (defined as adequate drainage to achieve resolution of infection without need for surgical drainage and with subsequent hospital discharge) compared with needle aspiration (96 versus 78 percent with needle aspiration). Catheter drainage also resulted in an average of one day shorter time to clinical improvement and to 50 percent decrease in abscess cavity size.

  Even very large abscesses (>10 cm, sometimes known as "giant abscesses") can be successfully managed with catheter drainage, although the risk of treatment failure and other complications is substantial whatever the approach [3,56,57]. In a single-center study from Singapore that included 44 pyogenic liver abscesses >10 cm in diameter, 39 were treated with percutaneous drainage [56]. Of those, 25 percent experienced a complication, including death from sepsis, pleural effusion requiring drainage, and need for repeat percutaneous drainage.

  Some studies have suggested that abscess size >5 cm is associated with failure of percutaneous drainage [58,59]. In one retrospective study of 80 patients with abscess >5 cm, the rate of treatment failure was lower with surgical drainage (7 versus 28 percent), but there were no differences in mortality, morbidity, duration of fever, or complication rates with percutaneous versus surgical drainage [59].

- **Multiple or multiloculated abscesses** – The decision on drainage approach for multiple or multiloculated abscesses should be made on an individual basis by a multidisciplinary team taking into account the number, size, and accessibility of the abscess(es), the experience of the surgeons and radiologists, and the underlying condition and comorbidities of the patient. Surgical drainage (open or laparoscopic) has been the traditional approach for these circumstances, but in some specific cases, multiple or loculated abscesses may be successfully managed by percutaneous drainage, particularly when the abscesses are small and easily accessible percutaneously. This was illustrated in one retrospective study that described successful percutaneous drainage in the setting of multiple abscesses (22 of 24 patients) and multiloculated abscesses (51 of 54 patients) [60].

Surgical drainage is indicated for patients who have an inadequate response to percutaneous drainage after seven days or who have abscesses with viscous contents obstructing the drainage catheter.

Successful medical treatment of liver abscess without drainage or aspiration has been described, but only in a few patients, and the patient characteristics associated with good outcomes with medical therapy alone are unknown [61,62].

Antibiotic therapy — No randomized controlled trials have evaluated antibiotic regimens for treatment of pyogenic liver abscess. Treatment recommendations are based upon the probable source of infection and should be guided by local bacterial resistance patterns, if known. (See 'Microbiology' above.)

Empiric therapy — Empiric broad-spectrum parenteral antibiotics should be administered pending aspiration of the abscess and microbiologic analysis of the abscess contents. The empiric regimen should cover streptococci, enteric gram-negative bacilli, and anaerobes. The empiric regimen should also cover *E. histolytica* until the causative pathogen(s) is found or amebic abscess is excluded.

Our preferred regimens include the following. Doses are found in the table (table 1):

- A third or later generation cephalosporin plus metronidazole
- A beta-lactam-beta-lactamase inhibitor combination (eg, piperacillin-tazobactam) with or without metronidazole (the metronidazole would be to provide *E. histolytica* coverage). In general, we avoid ampicillin-sulbactam and amoxicillin-clavulanic acid due to rising rates of resistance of *E. coli* and other gram-negative bacteria to these agents; local rates of resistance should be reviewed before prescribing.

- Ampicillin plus gentamicin plus metronidazole. We typically discontinue the gentamicin after 48 to 72 hours and replace it with a different agent if necessary.

Alternative regimens include:

- A fluoroquinolone with metronidazole
- A carbapenem with or without metronidazole (the metronidazole would be to provide *E. histolytica* coverage)

If the patient is in septic shock or if *S. aureus* is a concern (eg, in a patient with an indwelling vascular catheter or recent injection drug use), we typically add vancomycin.

The rationale for our regimen preferences includes predicted efficacy based on expected spectrum of activity as well as antimicrobial stewardship concerns. The choice among these options also depends on patient circumstances (such as allergy or expected tolerability, history of prior antimicrobial use) and drug toxicity, interactions, availability, and cost. In addition, if a biliary source is possible, we are more likely to choose a regimen with enterococcal coverage (eg, piperacillin-tazobactam or ampicillin plus gentamicin plus metronidazole).

Directed therapy and duration — Once culture and susceptibility results from blood and abscess specimens are available, the antibiotic regimen can be tailored accordingly. However, sometimes directed therapy warrants continued polymicrobial coverage, even if only a single organism is isolated. As an example, some experts continue polymicrobial coverage if the only organism isolated is a viridans group streptococcus other than *S. anginosus*, *S. constellatus*, and *S. intermedius*.

All the regimens listed for empiric therapy of pyogenic liver abscess have coverage against streptococci, gram-negative pathogens, and anaerobes (table 1). If *S. aureus* or a *Candida* species is the only organism isolated, we narrow the regimen to cover only that organism because isolation of these organisms is less likely to reflect a polymicrobial abscess. (See "Clinical approach to Staphylococcus aureus bacteremia in adults", section on 'Management'.)

If there are no revealing microbiologic data and no other pathogens suspected, we continue the empiric regimen for directed therapy. The exception to this is if a gentamicin-containing regimen was used for empiric therapy, as we don't continue gentamicin for more than 72 hours; in such cases, we switch to one of the other preferred empiric regimens for the remainder of the course.

Regardless of whether a causative organism has been identified, antibiotic therapy for four to six weeks total is usually recommended [63]. Patients who have had a good response to initial

drainage should be treated with two to four weeks of parenteral therapy, while patients with incomplete drainage should receive four to six weeks of parenteral therapy. The remainder of the course can then be completed with oral therapy tailored to culture and susceptibility results [53,54]. If culture results are not available, reasonable empiric oral antibiotic choices include amoxicillin-clavulanate alone (875 mg/125 mg every eight hours) or a fluoroquinolone (ciprofloxacin 500 mg twice daily or levofloxacin 750 mg once daily) plus metronidazole.

In some cases, a shorter time to step down to oral therapy is sufficient. In a randomized trial of 152 patients with *K. pneumoniae* liver abscess, most of whom had drainage, rates of clinical cure at 12 weeks were similar with a stepdown to oral ciprofloxacin after five to seven days of parenteral therapy compared with continuing parenteral therapy (96 versus 92 percent); each was given for a total of 28 days, followed by additional oral antibiotics, if necessary [64]. However, it is uncertain whether these results can be generalized to other pathogens and other settings, particularly with polymicrobial infections.

The specific duration of antibiotic therapy is typically determined by the extent of infection, the patient's clinical response to initial management, and comorbidities. Patients with abscesses that are not drained or are suboptimally drained usually require longer courses. Other useful clinical indicators to follow are pain, temperature, white blood cell count, and serum C-reactive protein.

Follow-up — We suggest **not** doing follow-up imaging, unless the patient has persistent clinical symptoms or drainage is not proceeding as expected. Radiological abnormalities resolve much more slowly than clinical and biochemical markers, so imaging may cause unwarranted alarm and unnecessary continuation or escalation of treatment interventions. Among 102 pyogenic liver abscess patients in Nepal, most of whom did not undergo abscess drainage, the mean time to ultrasonographic resolution of abscesses <10 cm was 16 weeks; mean time to resolution for abscesses >10 cm was 22 weeks [65].

Patients who have persistent clinical symptoms with ongoing evidence of an abscess on imaging following attempted drainage and antibiotic therapy require reevaluation for repeated drainage. Surgical intervention is indicated if this is not technically possible.

PROGNOSIS

The mortality rate in developed countries ranges from 2 to 12 percent [3,17]. Independent risk factors for mortality include need for open surgical drainage, the presence of malignancy, and the presence of anaerobic infection [66,67]. Access to optimal diagnostic and intervention

resources will almost certainly be critical to the outcome. There are few published outcome data from low-resource settings.

SUMMARY AND RECOMMENDATIONS

- **Pathogenesis** – Pyogenic liver abscesses usually develop in the context of biliary disease, portal pyemia, arterial hematogenous seeding, or via direct spread. (See 'Pathogenesis' above.)

- **Microbiology** – Most pyogenic liver abscesses are polymicrobial, with enteric gram-negative bacilli and anaerobic species predominating. In East Asia, monomicrobial infection with *Klebsiella pneumoniae* is an important cause of primary liver abscess. (See 'Microbiology' above and "Clinical features, diagnosis, and treatment of Klebsiella pneumoniae infection".)

- **Clinical manifestations** – The common clinical manifestations of pyogenic liver abscess are fever and abdominal pain; other symptoms may include nausea, vomiting, anorexia, weight loss, and malaise. (See 'Clinical manifestations' above.)

- **Diagnosis** – Evaluation of suspected pyogenic liver abscess includes imaging (usually CT or ultrasound), blood cultures, and aspiration for culture of the abscess material. The diagnosis is confirmed in a patient with a liver lesion on imaging that is purulent on aspiration and/or has bacteria identified on Gram stain or culture of the aspirate material or blood (image 2). (See 'Diagnosis' above.)

  If bacterial pathogens are not identified on routine microbiologic evaluation, clinicians should consider possible "atypical" pathogens. The primary infectious differential diagnosis for pyogenic liver abscess is amebic liver abscess, caused by *Entamoeba histolytica.* This is best distinguished by serology or aspirate specimen testing (eg, antigen or molecular testing) for *E. histolytica*. (See 'Differential diagnosis' above.)

- **Role of drainage** – Most liver abscesses are treated with CT or ultrasound-guided percutaneous drainage, ideally with the placement of a drainage catheter. Other options are surgical drainage, open or laparoscopic, by endoscopic drainage or via endoscopic retrograde cholangiopancreatography. (See 'Drainage' above.)

  - For patients with a single unilocular abscess, we suggest percutaneous drainage (**Grade 2B**):

- Single abscesses ≤5 cm in diameter can be drained via needle aspiration with or without subsequent placement of a drainage catheter. The choice depends on availability and operator preference. If only needle aspiration is performed, repeat aspiration may be required for complete resolution.

- For drainage of single abscesses >5 cm in diameter, we suggest percutaneous catheter drainage for all (**Grade 2B**). Drainage catheters should remain in place until drainage ceases (usually up to seven days).

- For patients with multiple or multiloculated abscesses, the drainage approach depends on the number, size, and accessibility of the abscess(es), the experience of the surgeons and radiologists, and the underlying condition and comorbidities of the patient. Surgical drainage has been the traditional approach, but some multiple or multiloculated abscesses can be successfully managed by percutaneous catheter drainage.

- Surgical drainage is appropriate when there is an underlying disease that requires primary surgical management, when there is an inadequate response to catheter drainage, or if the abscess has viscous contents precluding successful percutaneous drainage.

- **Antimicrobial therapy** – Clinicians should treat with empiric broad-spectrum parenteral antibiotics following aspiration of the abscess. Treatment will then be guided by the microbiologic findings. We suggest an empiric regimen that covers streptococci, gram-negative bacilli, and anaerobes (**Grade 2C**). Until *E. histolytica* has been reasonably excluded, we suggest that metronidazole be part of the empiric regimen (**Grade 2C**). Suggested regimens are outlined in the table (table 1). (See 'Empiric therapy' above.)

  Once culture and susceptibility results from blood and drainage specimens are available, the antibiotic regimen can be tailored appropriately. Antibiotics are generally continued for four to six weeks total, depending on the clinical response to therapy. (See 'Directed therapy and duration' above.)

- **Limited role of follow-up imaging** – We suggest **not** doing routine follow-up imaging. We only obtain follow-up imaging if there are persistent clinical symptoms or if drainage is not proceeding as expected. (See 'Follow-up' above.)

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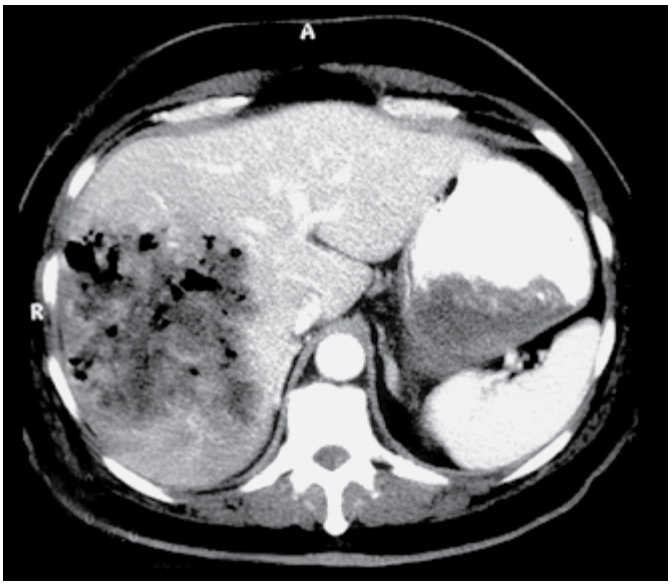
Topic 2680 Version 24.0

GRAPHICS

Liver abscess



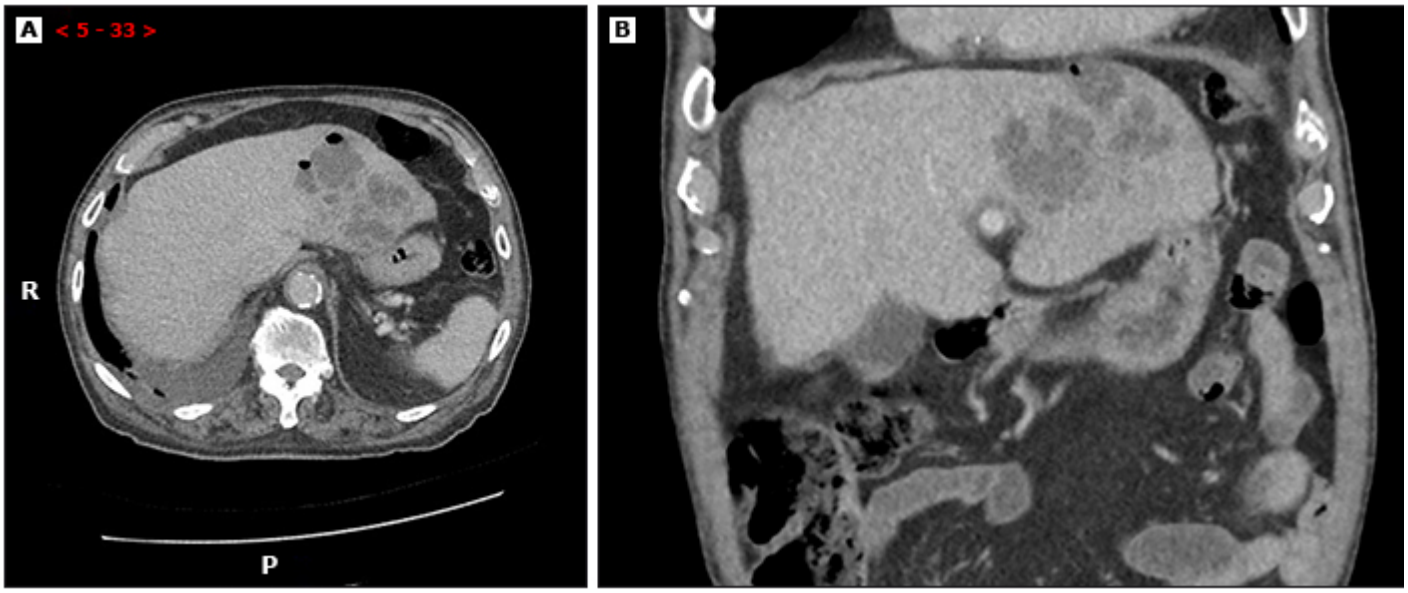
A contrast-enhanced CT scan of the upper abdomen demonstrates a large gas-containing abscess in the right lobe of the liver. This location is easily amenable to percutaneous CT-guided drainage.

CT: computed tomography.

Courtesy of Jonathan Kruskal, MD, PhD.

Graphic 61510 Version 3.0

Computed tomography images of a pyogenic liver abscess



Axial (A) and coronal (B) views of an air-containing, multiloculated pyogenic liver abscess caused by *Klebsiella pneumoniae*.

Courtesy of Joshua Davis, PhD, MBBS, FRACP, and Malcom McDonald, PhD, FRACP, FRCPA.

Graphic 119007 Version 1.0

Antibiotic regimens for pyogenic liver abscess

Regimen	Dose (adult)*
Preferred[¶]	
Beta-lactam/beta-lactamase inhibitor:[Δ]	
Piperacillin-tazobactam	3.375 or 4.5 g IV every six hours[◇]
Ticarcillin-clavulanate[§]	3.1 g IV every four hours
Third generation cephalosporin[¥] **PLUS metronidazole:**	
Ceftriaxone **plus**	2 g IV once daily
Metronidazole	500 mg IV or orally every eight hours
Ampicillin PLUS gentamicin PLUS metronidazole:	
Ampicillin **plus**	2 g IV every four to six hours
Gentamicin **plus**	5 to 7 mg per kg IV daily[‡]
Metronidazole	500 mg IV or orally every eight hours
Alternative regimens[¶]	
Fluoroquinolone PLUS metronidazole:	
Ciprofloxacin **or**	400 mg IV every 12 hours or 750 mg orally twice daily
Levofloxacin **plus**	500 or 750 mg IV or orally once daily
Metronidazole	500 mg IV or orally every eight hours
Carbapenem:[¶ †]	
Imipenem-cilastatin	500 mg IV every six hours
Meropenem	1 g IV every eight hours
Ertapenem	1 g IV once daily

An empiric antibiotic regimen for pyogenic liver abscess should cover streptococci, enteric gram-negative bacilli, and anaerobes.

IV: intravenous.

* Antibiotic doses should be adjusted appropriately for patients with renal insufficiency or other dose-related considerations.

¶ If the patient is in septic shock or if *Staphylococcus aureus* is a concern (eg, in a patient with an indwelling catheter or prior injection drug use), we typically add vancomycin. Refer to other UpToDate content for vancomycin dosing.

Δ These regimens have anaerobic activity without the addition of metronidazole. Unless involvement of *Entamoeba histolytica* is unlikely (eg, in patients with obvious biliary disease predisposing to pyogenic abscess), metronidazole 500 mg IV or orally every eight hours should be added until the causative organism has been identified or amebic serology or antigen testing has come back negative.

◇ The dose of 4.5 g every six hours should be used when *Pseudomonas* coverage is desired.

§ Ticarcillin-clavulanate is not available in the United States or Canada and is of limited availability in other locations.

¥ Cefepime is an additional cephalosporin choice and has expected activity against *Pseudomonas* when used at a dose of 2 g IV every eight hours.

‡ We do not continue a gentamicin-containing regimen for pyogenic liver abscess beyond 48 to 72 hours. If microbiologic data are unrevealing and a gentamicin-containing regimen was used for empiric therapy, we switch to one of these other empiric regimens to complete the antibiotic course. Refer to other UpToDate content about details on dosing for parenteral aminoglycosides.

† Carbapenems are typically reserved for patients who should not use other options because of drug allergies or concern for resistant infection. Ertapenem lacks activity against *Acinetobacter* and *Pseudomonas* and, of the carbapenems, is not an appropriate choice for severe or nosocomial infection.

Graphic 117437 Version 3.0

Contributor Disclosures

Joshua Davis, PhD, MBBS, FRACP No relevant financial relationship(s) with ineligible companies to disclose. **Malcolm McDonald, PhD, FRACP, FRCPA** No relevant financial relationship(s) with ineligible companies to disclose. **Stephen B Calderwood, MD** Consultant/Advisory Boards: Day Zero Diagnostics [Whole genome sequencing for microbial identification and determination of antimicrobial susceptibility]. All of the relevant financial relationships listed have been mitigated. **Keri K Hall, MD, MS** No relevant financial relationship(s) with ineligible companies to disclose.

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Conflict of interest policy

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