The Management of Hepatic Abscess

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Hepatic abscesses are the most common type of visceral abscess. In the United States the incidence rate is around 3 per 100,000 and is higher in men than women. Without prompt recognition and treatment, liver abscesses are uniformly fatal.

Hepatic abscesses can be divided into three major categories: pyogenic, amebic, and fungal. Pyogenic abscesses are caused primarily by polymicrobial aerobic and anaerobic bacteria from the gastrointestinal tract. Common risk factors include diabetes, underlying hepatobiliary disease including malignancy, and liver transplantation.

Amebic abscesses are the result of *Entamoeba histolytica,* which has a high endemic prevalence in Mexico, the Indian subcontinent, Indonesia, and Africa. Most patients with amebic liver abscesses in the United States have a history of recent travel to an endemic area.

Fungal abscesses are increasing in frequency, particularly in immunocompromised patients with a cancer or history of solid organ or bone marrow transplant. They typically are caused by *Candida* species.

The treatment of liver abscesses has evolved. Many nonoperative treatment strategies are available, and a multidisciplinary management approach from interventional radiologists, biliary endoscopists, and infectious diseases specialists can be successful in most cases. However, surgery remains the definitive treatment for large, complicated abscesses or when less invasive approaches fail.

PYOGENIC LIVER ABSCESS

Pyogenic abscesses are a rare but highly morbid disease. Over time there have been shifts in cause. Early in the twentieth century, pylephlebitis, from appendicitis, was the most common cause, with an overall mortality rate that approached 75% to 80%. During the 1950s to 1970s, biliary obstruction from benign and malignant diseases accounted for most of the cases. Recently, the landscape has shifted again with the emergence of liver transplantation as treatment for end-stage liver disease and hepatic malignancy.

Pathophysiology

Pyogenic abscesses can arise from multiple sources: (1) the biliary ductal system from ascending cholangitis, (2) the portal blood flow, from pylephlebitis originating from appendicitis or diverticulitis, (3) direct extension from adjacent disease, such as cholecystitis, (4) injury from trauma or liver-directed therapy, (5) the hepatic artery, from septicemia originating from a distant source, and (6) a cryptogenic process. In one of the largest Western series at the Johns Hopkins Hospital, 40% of pyogenic liver abscesses were biliary in origin, and an underlying malignant disease was the cause in the majority of these patients in the nontransplant setting.

In liver transplant recipients, additional risk factors for pyogenic abscess include: (1) hepatic infarction from vascular thrombosis or anastomotic stenosis, (2) ischemic cholangiopathy (nonanastomotic biliary stricture) as a consequence of hepatic arterial compromise or the use of deceased-donor liver organs procured after cardiac death (donation after circulatory death; Figures 1 and 2), and (3) biliary anastomotic stricture. The use of partial liver grafts (from live and deceased donors) carries an increased risk of biliary leak from the cut surface of the liver that may result in perihepatic pyogenic abscess. Although the infectious organisms and initial diagnostic and treatment algorithms are similar to non–transplant-related causes, the definitive treatment is based on patency of the hepatic vessels, viability of the bile ducts, and function of the hepatic allograft. In severe cases, retransplantation of the liver is the only option.

The microbiology is highly variable and depends on the underlying process (Table 1). *Escherichia coli*, *Klebsiella* spp., and *Enterococcus* spp. commonly are isolated in cases related to choledocholithiasis, whereas *Pseudomonas* spp., other multiple resistant gram-negative aerobes, vancomycin-resistant *Enterococcus* (VRE) spp., and yeast are the more likely pathogens in patients with biliary obstruction from malignancy who received multiple courses of antibiotics. Although cases with liver abscesses from diverticulitis and appendicitis are attributed to gram-negative aerobes and *Bacteroides fragilis,* patients with severe forms of cholecystitis are likely to harbor anaerobes such as *Clostridium perfringens* and *Bacteroides* spp. Other pathogens frequently associated with specific conditions are *Staphylococcus* spp. and methicillin-resistant *Staphylococcus aureus* (MRSA) from subcutaneous abscess, enterococcal and staphylococcal pathogens from endocarditis, and anaerobes in cryptogenic abscesses.

Diagnosis

The classic initial symptom of a pyogenic hepatic abscess is fever, which occurs in more than 90% of patients. Approximately one half of those with an abscess have abdominal or right upper quadrant pain. Other frequent symptoms include malaise, anorexia, and nausea. Occasionally, the diaphragm is involved, resulting in pleuritic chest pain, cough, or dyspnea. The mode of presentation also may include severe sepsis in patients with an underlying biliary malignancy and after liver-directed therapy or liver transplantation. On physical examination, the liver may be tender and enlarged, or the patient may appear jaundiced. Pyogenic liver abscesses rarely rupture, and frank peritonitis is unusual.

Over the past 40 years, advances in imaging have dramatically improved the diagnosis of pyogenic hepatic abscesses. Plain films may show an elevated right hemidiaphragm, right pleural effusion, right lower lobe atelectasis, abnormal extraluminal gas in the right upper quadrant, or portal venous gas if pylephlebitis is the source. Ultrasound (US) is a useful initial screening study for hepatic abscess because it has a sensitivity of 80% to 95% and is excellent in evaluation of the gallbladder and intrahepatic bile ducts. Computed tomography (CT) is more sensitive (95% to 100%) in the detection of abscesses, and the presence of gas and rim enhancement with intravenous contrast is suggestive of a hepatic abscess. CT also allows for a more thorough evaluation of the abdomen for detection of the underlying cause. Magnetic resonance imaging (MRI) of the liver is an equally sensitive technique in detection of liver abscesses and, in combination with magnetic resonance cholangiopancreatography, provides detailed information with regard to the relationship of the hepatic abscess to the biliary system.

Blood cultures should be drawn because they are positive in up to 50% of cases. Cultures obtained directly from an aspirate are critical, and both aerobic and anaerobic cultures should be requested. Cultures from existing drains are not appropriate because they typically are contaminated with skin flora and environmental organisms and will lead to misguided therapy.

Treatment

Pyogenic hepatic abscesses are associated with a significant mortality rate, and prompt diagnosis and treatment of hepatic abscesses are crucial for good outcomes. Management must include treatment of the liver abscess and the underlying source. Most pyogenic hepatic abscesses are managed with antibiotic administration and drainage.

Antibiotics

When a pyogenic hepatic abscess is suspected, first blood cultures should be drawn and then empiric intravenous antimicrobial therapy initiated. The antibiotic coverage subsequently is modified on the basis of results of blood cultures and a fluid sample from the abscess. As outlined previously, the bacteria found usually correspond to the source (see Table 1). As such, the choice of the initial antibiotic agents should be based on the presumed source of the hepatic abscess. For a presumed colonic source, the combination of fluoroquinolone or a third-generation cephalosporin with metronidazole provides appropriate coverage. For a presumed biliary source, a broad-spectrum penicillin such as piperacillin-tazobactam is a good choice and as empiric treatment for most gram-negative aerobes, anaerobes including *Clostridia* spp., and susceptible enterococcal species. If the patient is severely ill and has had recurrent cholangitis, meropenem to treat drug-resistant gram-negative bacteria and linezolid to treat VRE are reasonable choices. In liver transplant recipients, coverage for *Candida* spp. with fluconazole or an echinocandin should be considered. If a subcutaneous abscess or endocarditis is the presumed source, inclusion of vancomycin for MRSA coverage is appropriate.

If specific bacteria are isolated and sensitivities are determined, the antibiotic regimen should be targeted. Classically, antibiotic treatment has been recommended for 4 to 6 weeks; however, shorter antibiotic duration may be appropriate if adequate drainage has been achieved. Even when prolonged antibiotics are indicated for multiple small abscesses with no abdominal source, oral antibiotics with good bioavailability may be substituted for home intravenous antibiotics.

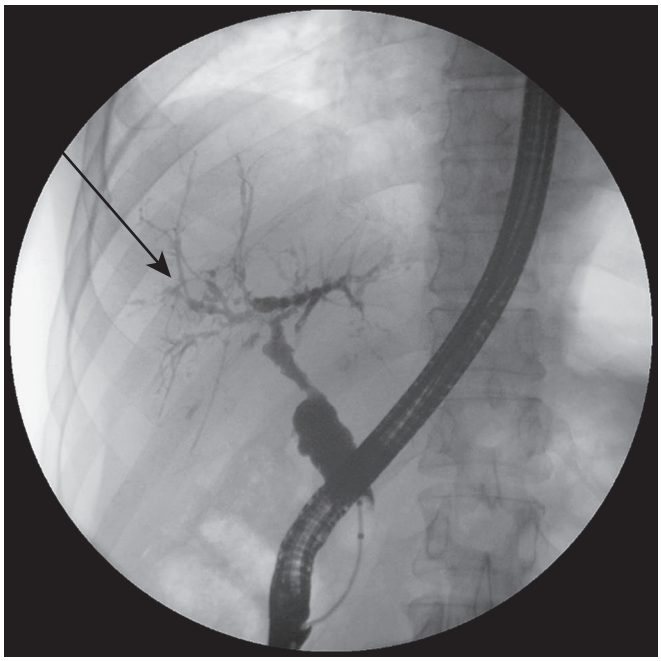

FIGURE 1 An endoscopic retrograde cholangiopancreaticography showing intrahepatic ischemic cholangiopathy after orthotropic liver transplantation with a graft procured after circulatory death.

TABLE 1: Underlying Processes and Typical Pathogens

Underlying Process	Typical Pathogens
Biliary, benign	• *Escherichia coli* • Anaerobes • *Klebsiella* spp. • *Enterococcus* spp.
Biliary, malignant	• *Pseudomonas* spp. • Multidrug-resistant GN aerobes • VRE • Yeast
Diverticulitis/appendicitis	• GN aerobes • *Bacteroides fragilis*
Severe cholecystitis	• See Biliary, benign • *Clostridium perfringens* • *Bacteroides* spp.
Subcutaneous abscess	• *Staphylococcus* spp. • MRSA
Endocarditis	• *Enterococcus* spp. • *Staphylococcus* spp.
Cryptogenic anaerobes	• Anaerobes

GN, Gram-negative; *MRSA,* methicillin-resistant *Staphylococcus aureus*; *VRE,* vancomycin-resistant *Enterococcus.*

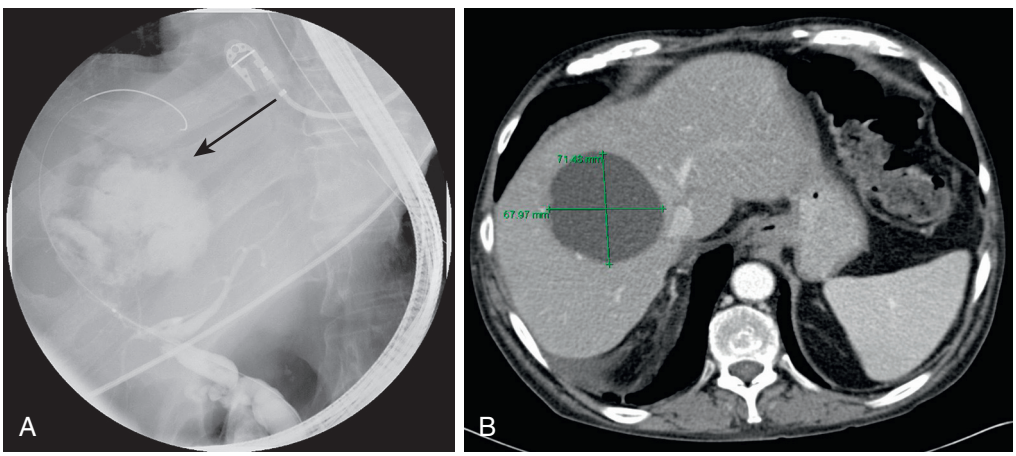

FIGURE 2 **A,** Endoscopic retrograde cholangiopancreaticography. **B,** Computed tomographic scan showing intrahepatic ischemic cholangiopathy progression to biloma and abscess formation.

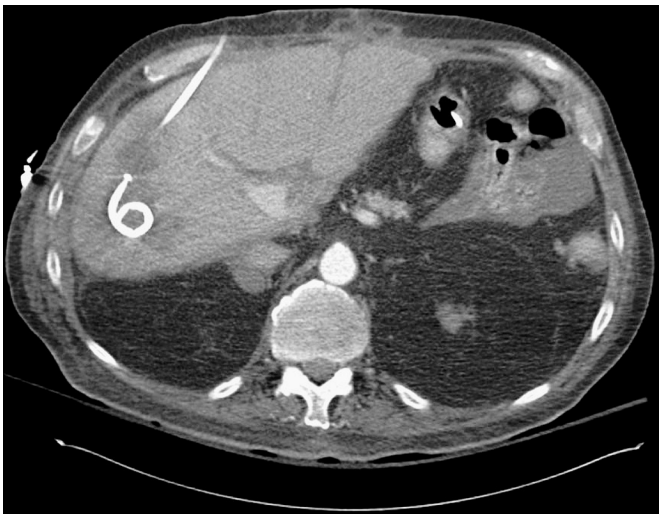

FIGURE 3 Radiograph showing percutaneous drainage of pyogenic abscess.

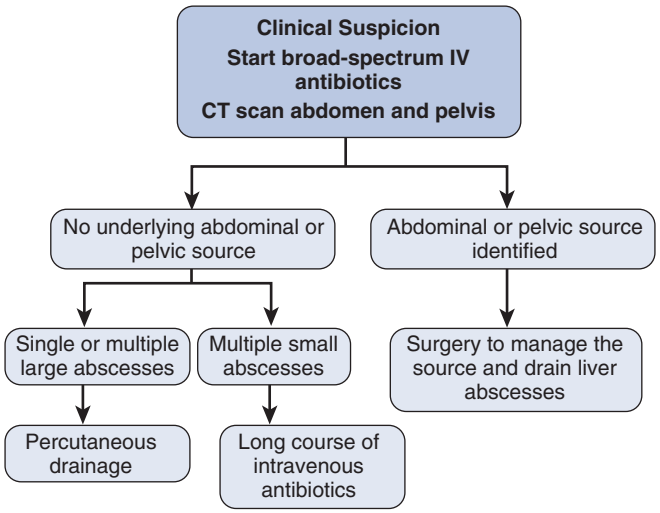

FIGURE 4 Algorithm for management of pyogenic hepatic abscesses. *CT,* Computed tomographic scan; *IV,* intravenous.

Drainage

Intravenous antibiotics have decreased the mortality rate of patients with pyogenic hepatic abscesses; however, most patients also need abscess drainage, either with percutaneous catheter placement, closed aspiration, or surgery. The surgical therapy of liver abscess has evolved to a multispecialty approach with advances in minimally invasive surgery, ablative therapies, and image-guided interventions.

Once the pyogenic abscess has been confirmed with imaging and no intra-abdominal source necessitates operative intervention, the initial management should include antibiotics and percutaneous drainage. At the Johns Hopkins Hospital from 1973 to 1993, 45% of patients were treated with a percutaneous drain; many of these cases, especially later in the series, involved multiloculated abscesses. Rajak and colleagues (1998) compared catheter placement with percutaneous aspiration and found that the success rate was superior with catheter placement (60% vs 100%). Percutaneous catheter placement involves the insertion of an 8F to 14F pigtail catheter over a guidewire with imaging guidance. The abscess cavity then is studied with the injection of contrast through the catheter. Finally, the catheter is left to gravity or suction, until complete resolution of the drainage and collapse of the abscess cavity have occurred (Figure 3). Percutaneous drainage is not appropriate for patients with multiple large abscesses, a known intra-abdominal source that requires surgery, ascites, or in whom transpleural drainage is required.

Percutaneous needle aspiration involves imaging-guided drainage of the abscess without placement of the catheter. The benefits of needle aspiration are decreased cost, traumatic complications, and avoidance of drain discomfort. Yu and colleagues (2004) compared outcomes after aspiration and drainage of liver abscesses and showed equivalent results between the two treatment modalities. Although aspiration resulted in less liver trauma, patient discomfort, and cost, this approach was associated with a higher recurrence rate requiring repeated aspiration procedures compared with catheter drainage.

Although patients with small hepatic abscesses and no biliary obstruction respond to prolonged intravenous antibiotics without drainage, a select group of patients requires surgical intervention.

When an intra-abdominal source for the infection requires an operation, the liver abscess can be drained surgically in concert with management of the primary problem (Figure 4). Surgical treatment also is required in cases of failed nonoperative therapies and remains the salvage procedure.

Before the availability of systemic antibiotics, an extraperitoneal approach for surgical drainage was performed to avoid contamination of the peritoneum. The availability of modern antibiotics and the current technique of a transperitoneal approach via a midline or right subcostal incision provide direct access to the liver abscess, abdomen, and pelvis. After the underlying disease in the abdomen is addressed, the liver is evaluated, and the hepatic abscess is located with palpation and intraoperative US. The area to be drained then is isolated from the rest of the abdomen with towels, and aspiration of the abscess is performed to obtain fluid for culture (Figure 5). A tract then is created through the hepatic parenchyma toward the cavity, ideally to drain the abscess in a dependent fashion. Next, the cavity is irrigated and suctioned to remove purulence and minimize contamination. The tract then should be enlarged and the abscess débrided to break up any loculated pockets of purulence. A large-caliber drain is placed in the abscess cavity, and the perihepatic area around the abscess also may be drained; however, these drains are brought out through separate incisions. All hepatic abscesses should be cultured to direct antibiotic therapy. Pathologic examination also is recommended to evaluate for malignancy and to look for trophozoites of *E. histolytica*.

Although drainage of a liver abscess in combination with systemic antibiotic is successful in most cases, hepatic resection is necessary in unusual circumstances. In patients in whom an inflammatory mass develops as a result of multiple percutaneous drainage procedures or chronic biliary obstruction from multiple biliary drainage procedures that involve one hemiliver, a hemihepatectomy is necessary to remove the diseased portion of the liver. However, these patients are prone to profound sepsis with liver manipulation; therefore partial hepatectomy should be undertaken cautiously (Box 1).

AMEBIC HEPATIC ABSCESS

Amebiasis is a relatively common global parasitic infection caused by the protozoan *E. histolytica,* with the highest incidence in tropical and subtropical climates. Amebiasis typically affects men between the ages of 20 and 40 years. Although uncommon in the United States, amebic abscesses should be included in the differential diagnosis in patients with a history of travel to or immigration from endemic areas of the world and in the presence of human immunodeficiency virus.

The liver is the most common extraintestinal location of amebiasis, and amebic liver abscesses occur in 1% of patients with amebiasis. Human infestation occurs with the ingestion of a mature cyst in fecal contaminated food, water, or hands. Excystation occurs in the small intestine, and trophozoites are released and migrate to the large intestine. The trophozoites produce cysts, which are passed in the feces.

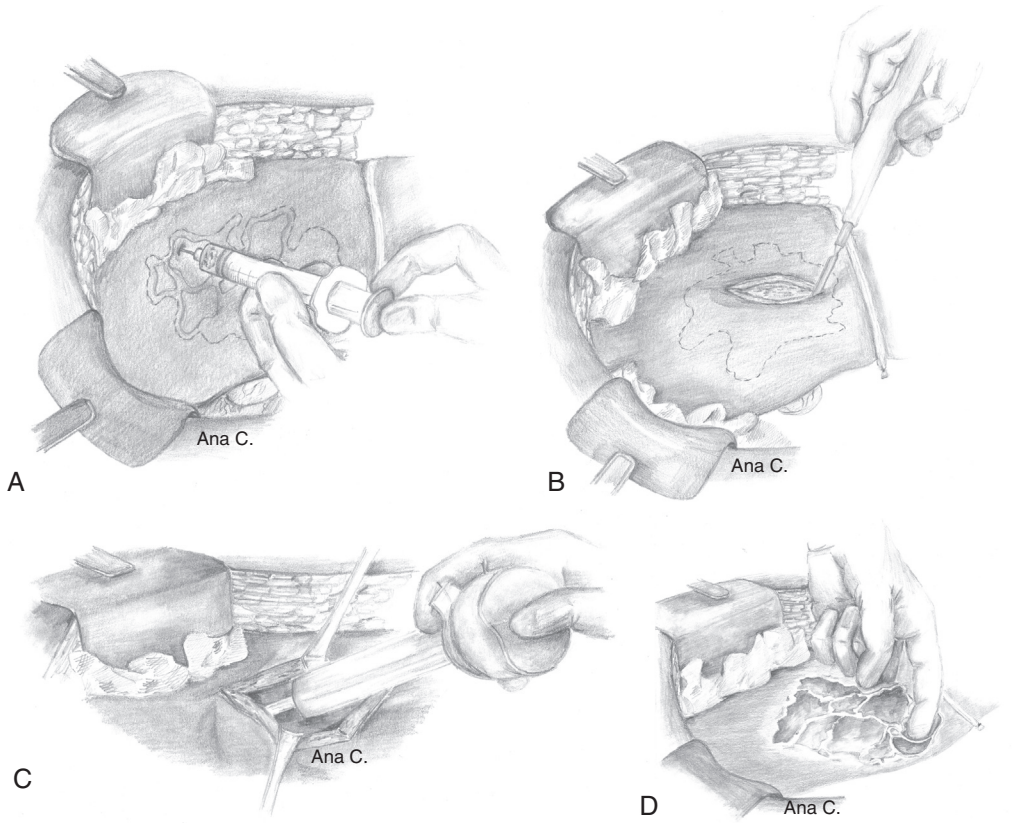

FIGURE 5 **A,** Abscess aspiration for aerobic and anaerobic culture. **B,** Incision of the liver capsule to drain the abscess. **C,** Irrigation of abscess cavity. **D,** Manual disruption of loculations. *(Illustrations by Ana Costache.)*

BOX 1: Pearls for Pyogenic Hepatic Abscesses

- The most common pathogens isolated from pyogenic liver abscess are gram-negative aerobes and anaerobic bacteria.
- With use of indwelling biliary stents, increasing antibiotic resistance, and growing numbers of immunocompromised patients, infection with fungal species, drug-resistant gram-negative organisms and gram-positive organisms, such as *Enterococcus,* also should be considered.
- Aspiration of liver abscess should be undertaken in most patients because it provides rapid relief of symptoms, microbiologic evaluation, and targeted antibiotic therapy.
- Percutaneous drainage usually is required, and open surgery should be reserved for selected patients.

In many cases, the trophozoites remain confined to the intestinal lumen of individuals who are asymptomatic carriers, passing cysts in their stool. In some patients, the trophozoites invade through the intestinal mucosa (intestinal disease), through the bloodstream, or via extraintestinal sites such as the liver, brain, and lungs (extraintestinal disease), where it forms into an abscess. The most common complication of amebic abscesses is rupture into the surrounding organs, such as direct extension into the pleuropulmonary space or rupture into the pericardium or peritoneum. The diagnosis and management of pyogenic and amebic abscesses differs, and these differences are reviewed.

Diagnosis

The presentation of amebic abscesses may be acute with fever and right upper quadrant pain or less specific with weight loss, fever, and abdominal pain. An amebic liver abscess usually does not present at the same time as colitis but within a year after the initial infection. Unlike a pyogenic abscess, the patient is not jaundiced and does not have underlying biliary disease. Also, most patients are younger than 50 years and have a history of travel to an endemic location. The definitive diagnosis of an amebic liver abscess is by identification of *E. histolytica* trophozoites in the pus or serum antibodies to the ameba. The majority of amebic liver abscesses (75% to 80%) show up as a single focus in the right lobe.

Treatment

With the introduction of metronidazole decades ago, drainage procedures (surgical or percutaneous) are only necessary in circumstances in which there are abscess complications, suspicion of bacterial coinfection, or diagnostic uncertainty.

Antibiotics

Treatment is based on amebicidal drugs to eliminate liver organisms and a luminal agent to eliminate intraluminal cysts even if not seen in the stool given the low sensitivity of microscopy to identify organisms. Preferred tissue agents include metronidazole 500 to 750 mg three times a day for 7 to 10 days. Tinidazole 2 g orally for 5 days is an alternative that may be better tolerated. To eradicate intraluminal cysts, the following regimens can be used: paromomycin (25 to 30 mg/kg per day orally three times a day for 7 days), diiodohydroxyquin (650 mg orally three times a day for 20 days), or diloxanide furoate (500 mg orally three times daily for 10 days for adults). Metronidazole treats intestinal and extraintestinal sites. Failure to use a luminal agent after metronidazole in cases of amebic abscess results in a 10% relapse rate.

BOX 2: Pearls for Amebic Liver Abscesses

- Only 10% to 20% of patients with amebic liver abscess have a history of diarrhea.
- Treatment should include an agent to target hepatic infection (e.g., metronidazole) as well as an intraluminal infection (e.g., paromomycin) to prevent relapse of amebic liver abscess.
- Failure to show response to antiamebic medication requires evaluation for polymicrobial infection with bacteria.
- Amebic abscess usually responds rapidly to antimicrobial therapy in 3 to 7 days, although follow-up imaging should be obtained and make take months to show resolution.
- Percutaneous drainage rarely is required.

Drainage

Blessmann and colleagues (2003) performed a prospective randomized trial to determine whether any significant benefit was obtained by adding aspiration to antibiotics for the treatment of amebic abscesses. In this study, aspiration did not improve the outcomes; therefore image-guided percutaneous treatment is used only in the following circumstances: (1) if no clinical response is seen after 5 to 7 days of antibiotics, and (2) if an abscess, especially a large one, is at high risk for rupture. If the complication of rupture or extension does occur, percutaneous drainage is useful in treating pulmonary, peritoneal, and cardiac complications. Although surgical drainage rarely is required for this disease, surgical intervention is required in unusual situations such as hemorrhage, erosion into surrounding organs, or sepsis from a secondarily infected amebic abscess that has failed percutaneous treatment.

Outcomes

The vast majority of patients with amebic abscesses respond after 3 days of therapy. However, if not treated in a timely fashion, this condition can be fatal, with mortality rates ranging as high as 15% to 20%. Several patient factors that are independent predictors of mortality include (1) a bilirubin value greater than 3.5 mg/dL, (2) encephalopathy, (3) an abscess volume greater than 500 mL, (4) an albumin value less than 2 g/dL, and (5) multiple abscesses. In addition, patients with complications of the abscess, rupture, or direct extension have worse outcomes. In conclusion, amebic abscesses respond well with medical management, and drainage procedures are reserved for rare circumstances. Clinical improvement precedes radiologic resolution, which may take up to 9 months. Follow-up imaging is advised (Box 2).

FUNGAL HEPATIC ABSCESS

The incidence of fungal liver abscesses has been increasing because of the increasing numbers of immunocompromised patients and increasing exposure to broad-spectrum antibiotics. Increased risk occurs with liver transplantation and bone marrow transplantation in particular as well as with hepatobiliary tumors. Mixed bacterial and fungal abscesses often occur in patients with biliary malignancies who have had indwelling stents and frequent exposure to antibiotic.

Treatment

Treatment of fungal abscesses follows the same principles as treatment for pyogenic hepatic abscesses, focusing on antimicrobial agents and drainage. Drainage is, again, with simple aspiration, percutaneous drainage, or surgical drainage. About 80% of fungal abscesses contain *Candida* spp.; the next most common fungal organisms are *Aspergillus* and *Cryptococcus*. Historically, amphotericin B was the first-line therapy, but micafungin and caspofungin are currently the agents of choice. An adequate course must be used; an earlier analysis suggested that inadequate treatment with amphotericin B was associated with a high mortality rate. Oral fluconazole may be used after initial intravenous therapy if *Candida albicans* is the cause. Patients with mixed fungal and bacterial abscesses also should receive appropriate antibiotics for the isolated bacteria.

Outcomes

Fungal abscesses of the liver are a significant source of mortality. The series from Johns Hopkins that analyzed fungal infections from 1973 to 1993 reported that all four patients with monomicrobial fungal abscesses with fungemia died. However, those patients who received a complete course of amphotericin B and did not have fungemia survived. In mixed fungal and bacterial abscesses, the overall mortality rate was 50%; however, adequate amphotericin B treatment resulted in a lower mortality rate (20% vs 62%). In conclusion, although fungal hepatic abscesses carry a high mortality rate, early administration of modern antifungal agents for the prevention of fungemia should improve survival.

SUGGESTED READINGS

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