

## Radiographic Highlights

# Pyogenic Hepatic Abscess

RADE B. VUKMIR, M.D., University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

SALVATORE A. DELUCA, M.D., coordinator of this series, is assistant professor of radiology at Harvard Medical School and associate radiologist at Massachusetts General Hospital, Boston.

**Pyogenic hepatic abscess is a rare condition associated with severe sequelae. The diagnosis may be obvious in patients with fever and leukocytosis who are clearly predisposed to this infectious complication. In patients without known risk factors, diagnosis and treatment are often delayed, usually until numerous health care resources have been consulted. The evaluation of occult hepatic abscess may be improved by a history directed at identifying predisposing conditions, by an appropriate physical examination and by the use of computed tomographic scanning. The standard treatment for pyogenic hepatic abscess is percutaneous or open drainage, accompanied by broad-spectrum antibiotic therapy.**

At the beginning of this century, hepatic abscess most often occurred secondary to appendicitis.<sup>1</sup> However, the predisposing factors for this rare infectious complication have changed, and morbidity and mortality have decreased as a result of improved diagnostic and treatment modalities.<sup>1-3</sup>

Hepatic abscesses occur in 0.12 percent of patients admitted to hospitals and are found in 0.41 percent of patients at autopsy.<sup>2,4</sup> In 90 percent of cases, these abscesses are caused by bacteria; the remaining 10 percent of cases are of amebic origin or unknown origin.<sup>2</sup> Bacterial (pyogenic) hepatic abscesses tend to be more fulminant than amebic abscesses (Table 1).<sup>2,3,5-8</sup>

Hepatic abscess can occur in persons of any age. However, the age distribution for this condition is bimodal, with peaks occurring in the first year of life and between 60 and 80 years of age.<sup>4</sup> The mean age of patients with hepatic abscess is 56.2 years.<sup>3,5</sup> This infectious complication is slightly more common in males (57.4 percent) than in females.<sup>9</sup>

The etiology of hepatic abscess is age-dependent.<sup>2,10</sup> In neonates, this condition most often occurs in association with sepsis and umbilical vein catheterization. In children, the predominant cause of hepatic abscess is Job syndrome or severe combined immunodeficiency disorder (chronic granulomatous disease). Trauma is the most common cause of this abscess in adolescents. Hepatic abscesses are usually related to biliary disease in adults and to malignancy in the elderly.

Certain medical conditions may predispose patients to the development of hepatic abscess. Among these are cardiopulmonary disease, diabetes mellitus, diverticulitis, inflammatory bowel disease,

TABLE 1

**Demographic Characteristics of Patients with Pyogenic and Amebic Hepatic Abscesses**

Characteristic	Pyogenic abscess	Amebic abscess
Age of patient	Older than 50 years	Younger than 50 years
Travel history	None	Endemic to Mexico
Presentation	Fulminant	Indolent
Symptoms	Fever Emesis Weight loss Night sweats Pleurisy	Malaise Diarrhea Nausea Anorexia
Signs	Painful abdominal mass Jaundice Sepsis	Hepatomegaly Splenomegaly
Diagnosis	Leukocytosis Anemia Elevated bilirubin level	Amebic serology
Mortality rate	40%	10%

Derived from references 2, 3 and 5 through 8.

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biliary disease, malignancy, aplastic anemia and sickle cell disease.<sup>5,6</sup>

### Symptoms and Signs

Symptoms associated with hepatic abscess include fever, nausea, vomiting, fatigue, rigor, weight loss, cough, pleuritic chest pain and night sweats.<sup>2,3</sup> Fever—probably the most common symptom—occurs in 87 to 100 percent of patients.<sup>2,7,11</sup> Body temperatures have been reported to range from 38.9° C to 41.0° C (102.0° F to 105.8° F). The fever follows a hectic, or “picket fence,” pattern that is typical of sepsis. In one study,<sup>5</sup> subjective sensations of anorexia and malaise were found to occur in 97 percent of patients.

Physical signs of pyogenic hepatic abscess include abdominal tenderness, hepatomegaly, jaundice and pulmonary abnormalities with associated clubbing, ascites and splenomegaly.<sup>2,5</sup> The most common physical finding is abdominal tenderness, which occurs in 71 percent of patients and is localized to the right upper quadrant in 65 percent of these patients.<sup>5</sup>

### Diagnosis

#### LABORATORY TESTS

The laboratory evaluation of pyogenic hepatic abscess almost always reveals leukocytosis. In 87 percent of patients, white blood cell counts range from 3,800

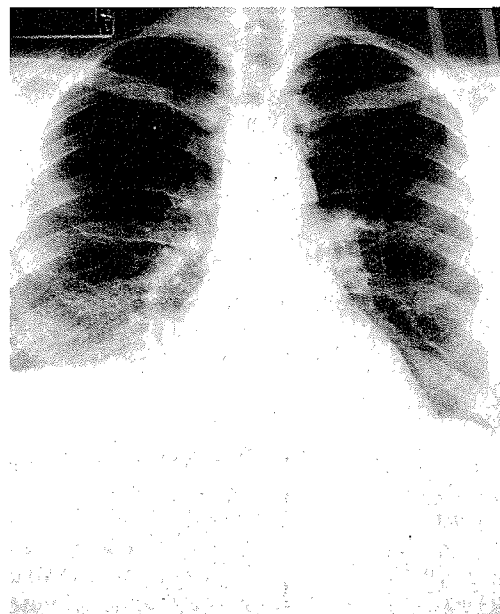


FIGURE 1. Chest radiograph showing hemidiaphragm elevation and pleural effusion in a patient with hepatic abscess.

to 41,000 per mm<sup>3</sup> (3.8 to 41.0 × 10<sup>9</sup> per L), with a mean of 17,000 per mm<sup>3</sup> (17.0 × 10<sup>9</sup> per L). A shift to immature cell forms occurs in 67 percent of these patients.<sup>3,6</sup>

Hematologic indices often reveal anemia of chronic disease. Normochromic, normocytic anemia, indicated by a mean hemo-

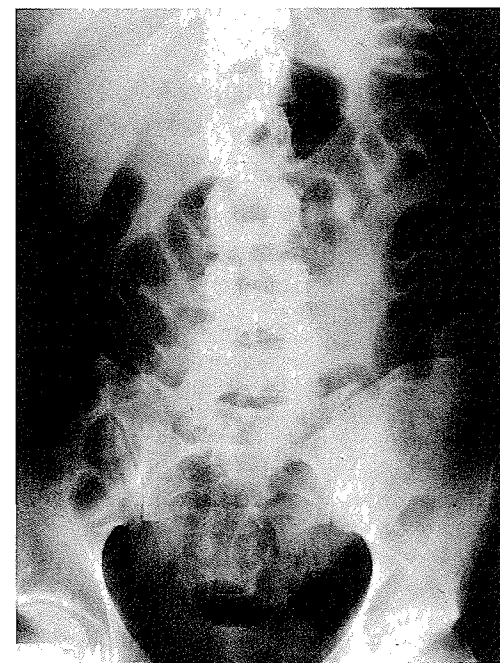


FIGURE 2. Abdominal radiograph demonstrating an abnormal bowel gas pattern due to enlargement of the liver in a patient with hepatic abscess.

### The Author

RADE B. VUKMIR, M.D.

is an assistant professor in the departments of anesthesiology/critical care medicine and emergency medicine at the University of Pittsburgh School of Medicine. He specializes in the intensive care of patients following trauma, neurosurgery and liver transplantation. Dr. Vukmir received his medical degree from the University of Pittsburgh, where he also completed a residency in emergency medicine and a fellowship in critical care medicine.

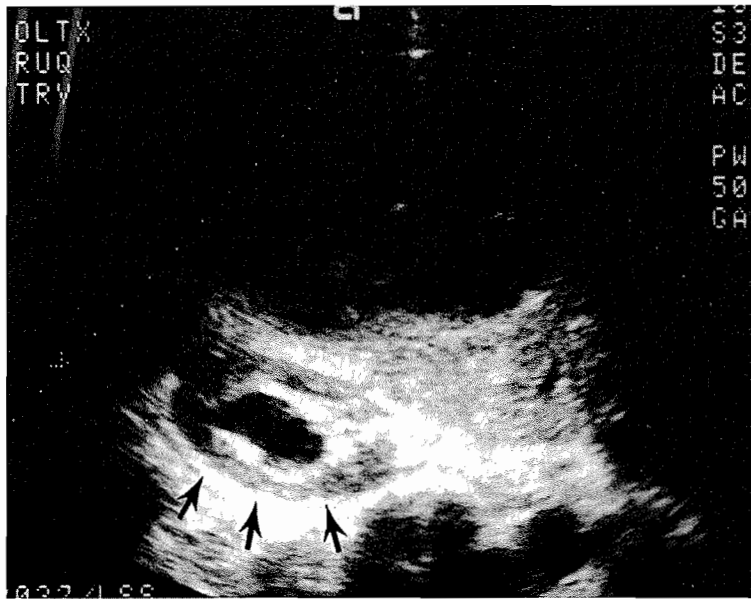


FIGURE 3. Ultrasonogram revealing a single hepatic abscess (arrows).

globin of 10 g per dL (100 g per L) and a hematocrit of 35 percent (0.35), occurs in 74 percent of patients with pyogenic hepatic abscess.<sup>3,6</sup>

Liver function studies demonstrate elevated alkaline phosphatase levels in 97 percent of patients with pyogenic hepatic abscess. The mean alkaline phosphatase level in these patients is 400 U per L. Aspartate aminotransferase and alanine aminotransferase levels may also be ele-



FIGURE 4. Ultrasonogram showing multiple hepatic abscesses (arrows).

vated.<sup>2,3</sup> An elevated total bilirubin level, with a mean value of 3.2 mg per dL (54  $\mu$ mol per L), implies hepatic structural collapse and resultant cholestasis. The finding of elevated bilirubin is a poor indicator of outcome, since it occurs in only 53 percent of patients.<sup>3,5</sup>

Other reported abnormalities include a decrease in the serum albumin level to less than 2.0 g per dL (20 g per L) and increases in both the prothrombin time and the erythrocyte sedimentation rate.<sup>2</sup>

Blood cultures are positive for bacteria in 50 percent of patients, and aspirates obtained from the abscesses are positive for bacteria in 73 percent of specimens.<sup>3,4,6</sup> Percutaneous aspiration of the abscess often yields a malodorous exudate, which indicates that the abscess is polymicrobial, rather than amebic, in etiology.

#### RADIOGRAPHS

Although the chest radiograph is abnormal in 41 to 53 percent of patients with pyogenic hepatic abscess (Figure 1), radiographic studies are neither sensitive nor specific for this condition.<sup>2,6</sup> The most common radiographic findings are right-sided hemidiaphragm elevation, pleural effusion with blunting of the costophrenic angle, and basilar atelectasis or infiltrate.<sup>2,3</sup>

Abdominal radiographs reveal abnormalities in only 19 percent of patients. The predominant abnormality seen on abdominal films is gastric displacement due to enlargement of the liver<sup>2</sup> (Figure 2).

#### ULTRASOUND SCANS

Ultrasound has a sensitivity of 80 percent for the detection of hepatic abscess. This study can reveal a hypoechoic area in an abscess as small as 1 cm in diameter<sup>6,12</sup> (Figures 3 and 4).

#### RADIONUCLIDE ISOTOPE SCANNING

Radionuclide isotope scanning uses labeled tracers that are concentrated in hepatocytes or reticuloendothelial cells.

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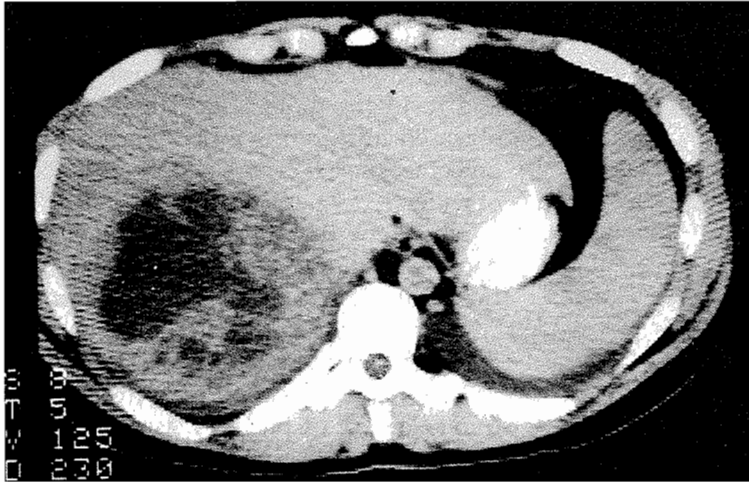


FIGURE 5. Abdominal CT scan showing a solitary abscess in the right lobe of the liver.

However, the use of these tracers may be limited in disease states that are associated with serum bilirubin levels greater than 5 mg dL (86  $\mu$ mol per L).<sup>12,13</sup>

A "cold" hepatobiliary scan performed with technetium sulfur colloid shows decreased uptake with 80 percent accuracy. "Hot" scans using gallium citrate-labeled or indium-labeled autologous leukocytes



FIGURE 6. Multiple hepatic abscesses on abdominal CT scan of the liver.

reveal increased uptake in lesions less than 2 cm in diameter with a sensitivity of 85 percent or 90 percent, respectively.<sup>13,14</sup>

## COMPUTED TOMOGRAPHY

Computed tomography (CT) is the preferred noninvasive diagnostic technique for pyogenic hepatic abscess. It has an overall sensitivity of 95 percent, with a sensitivity of 92 percent for single abscesses (Figure 5) and a sensitivity of 100 percent for multiple abscesses<sup>12,13</sup> (Figure 6).

## INVASIVE PROCEDURES

Endoscopic retrograde cholangiography and percutaneous transhepatic cholangiography are useful if biliary obstruction and ascending cholangitis are suspected. However, the use of these procedures carries the risk of dissemination of infection. Angiography is associated with fewer complications and may be 100 percent sensitive for hepatic abscesses in both children and adults.<sup>6,15</sup> The current diagnostic "gold standard" for pyogenic hepatic abscess is percutaneous aspiration guided by CT or ultrasound.

## Microbiology

Examination of access routes demonstrates that the biliary system is the most common route by which pathogens enter the liver (Table 2).<sup>2,4,9,16</sup> Pyogenic hepatic abscesses occur more commonly in the right lobe of the liver, which has increased biliary duct anastomoses and direct portal and superior mesenteric vein drainage; in contrast, the left lobe has only splenic vein drainage.<sup>11</sup> The right lobe is involved in 65 percent of patients with hepatic abscess. Both lobes are affected in 30 percent of patients, and the left lobe is affected in only 5 percent of patients.<sup>17</sup>

Hepatic abscesses resulting from bacterial, viral, mycotic, protozoal and amebic pathogens have been described. Bacteriologic analysis most commonly implicates gram-negative aerobic rods.<sup>4,9</sup> Gram-posi-

TABLE 2

## Etiology of Hepatic Abscess by Route of Entry

Route	Incidence	Etiology
Biliary	32%	Cholelithiasis Stricture Tumor
Idiopathic	22%	Unknown
Portal vein	22%	Appendicitis Diverticulitis Inflammatory bowel disease Omphalitis Peritonitis Tumor Splenic infection
Hepatic artery	14%	Endocarditis Pneumonia Pyelonephritis
Direct extension	5%	Gallbladder empyema Peptic ulcer Perihepatic abscess Perinephric abscess
Primary hepatic	5%	Foreign body Ischemia Parasites Trauma

Derived from references 2 through 4, 9 and 16.

tive aerobic cocci, including streptococci and staphylococci, are commonly found in hepatic abscesses in children.<sup>9,10</sup> Anaerobic pathogens include *Bacteroides*, *Clostridium* and *Peptostreptococcus* species.<sup>5</sup>

Recent studies<sup>2,18</sup> using improved culture techniques have found that gram-negative and anaerobic species may be less important in the etiology of spontaneous pyogenic hepatic abscess than was previously thought. These studies indicate that nonhemolytic streptococci or normal oral flora, including *Streptococcus sanguis*, *Streptococcus mitis*, *Streptococcus milleri*, *Streptococcus mutans* and *Streptococcus salivarius*, may play a more prominent role in this abscess.

*S. milleri* has been isolated from cultures

in 62.5 percent of patients with hepatic abscess.<sup>13</sup> This finding is important, because most streptococci are resistant to metronidazole (Flagyl), a drug that is commonly used to treat hepatic abscess.

### Treatment

Historically, surgical intervention has been the primary treatment for the solitary pyogenic hepatic abscess. Medical management is used for multiple abscesses, with the choice of drug therapy dependent on an analysis of the microbiologic spectrum (Table 3).<sup>5,6,19</sup>

### DRUG THERAPY

Drug therapy for pyogenic hepatic abscess previously was initiated with 20 to 40 million units of penicillin G. Ampicillin and the extended-spectrum penicillins—nafcillin (Nafcil, Unipen) or mezlocillin (Mezlin)—may be used to treat hepatic abscess due to streptococcal or staphylococcal infection.<sup>19,20</sup>

Abscesses caused by Enterobacteriaceae species are traditionally treated with an aminoglycoside, predominantly gentamicin (Garamycin) or tobramycin (Nebcin), or with a second-generation cephalosporin, usually cefoxitin (Mefoxin), cefotetan (Cefotan) or cefamandole (Mandol).<sup>6</sup>

Infections due to anaerobic organisms, predominantly *Bacteroides* species, respond well to clindamycin (Cleocin), metronidazole or a third-generation cephalosporin, such as cefotaxime (Claforan) or ceftizoxime (Cefizox).<sup>21</sup>

Broad-spectrum coverage was once provided by chloramphenicol (Chloromycetin). More recently, newer agents, such as ampicillin-sulbactam (Unasyn), ticarcillin-potassium clavulanate (Timentin) and imipenem-cilastatin (Primaxin), have been used in the treatment of pyogenic hepatic abscess. New pathogens, predominantly microaerophilic streptococci such as *S. milleri*, commonly emerge and are resistant to metronidazole.<sup>18</sup>

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TABLE 3

## Drug Therapy for Pyogenic Hepatic Abscess

<i>Pathogens</i>	<i>Antibiotic agents</i>
<b>Aerobic organisms</b>	
Gram-negative rods (44%) <i>Escherichia coli</i> <i>Klebsiella pneumoniae</i>	Treat with single agent: Ampicillin-sulbactam (Unasyn) or Ticarcillin-potassium clavulanate (Timentin) or Imipenem-cilastatin (Primaxin)
Gram-positive cocci (40%) Streptococcus species Staphylococcus species	Treat with two agents: Second- or third-generation cephalosporin <i>plus</i> metronidazole (Flagyl) or clindamycin (Cleocin) or Ampicillin <i>plus</i> chloramphenicol (Chloromycetin)
<b>Anaerobic organisms (8%)</b>	
Bacteroides species Clostridium species Peptostreptococcus species	Treat with three agents: Ampicillin or antipseudomonal penicillin <i>plus</i> a second- or third-generation cephalosporin or an aminoglycoside <i>plus</i> metronidazole or clindamycin
<b>Microaerophilic organisms (6%)</b>	
<i>Streptococcus milleri</i> <i>Streptococcus mitis</i>	Use same treatment as for anaerobic organisms

Derived from references 5, 6 and 19.

Antibiotic therapy should be continued for four to six weeks. Oral therapy may be used in the last two weeks if clinical improvement continues.<sup>21</sup> If the infection does not respond to intravenous drug therapy after 48 hours, an aspirate of the abscess should be obtained for culture and sensitivity studies.<sup>19</sup> Medical management has resulted in complete recovery in 21 to 100 percent of patients with pyogenic hepatic abscess.<sup>19,22</sup>

## SURGICAL PROCEDURES

Surgical intervention is warranted if a patient with pyogenic hepatic abscess does not respond to drug therapy within 48

hours or if the patient's clinical condition deteriorates.<sup>11</sup> Percutaneous aspiration and drainage are successful in 86 to 92 percent of patients.<sup>20,23</sup> If this technique fails, open surgical drainage is performed.<sup>23</sup> Surgical techniques include extraperitoneal drainage for hepatic dome abscess, transperitoneal drainage using a subcostal approach or posterior drainage using a transpleural approach.<sup>11</sup>

Similar mortality rates have been found for CT-guided percutaneous drainage (13 percent) and open surgical drainage (14 percent).<sup>6</sup> However, the morbidity rates (measured as the length of hospital stay) have been found to be 12 percent for CT-guided percutaneous drainage and 17 percent for open drainage.<sup>16</sup>

Thus, the standard of therapy for pyogenic hepatic abscess is CT-guided percutaneous drainage accompanied by broad-spectrum antibiotic therapy. When conservative therapy fails or the clinical condition warrants, open surgical drainage is performed.

## Prognosis

The prognosis for patients with pyogenic hepatic abscess is variable. Complications occur more frequently in infants, in the elderly and in patients with biliary disease.<sup>2,6</sup> The prognosis is strongly affected by the timeliness of diagnosis. In one study,<sup>3</sup> the diagnosis of pyogenic hepatic abscess was delayed an average of 38 days; cholangitis and fever of unknown origin were the most frequent erroneous diagnoses.

The mortality rate for patients with a single hepatic abscess is 45 percent, and the mortality rate for those with multiple abscesses is 77 percent.<sup>9</sup> Morbidity is considerable: hospital stays for patients with pyogenic hepatic abscess range from two to 107 days, with a median of 28 days. Abscess perforation occurs in 48 percent of patients, and a third of these patients develop septicemia.<sup>5,6,24</sup>