Acute Ascending Cholangitis

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Pancreatic cancer is the fourth leading cause of death in men and women in the United States. In 2003, Jemal et al. estimated that 30,700 people were diagnosed with pancreatic cancer and 30,000 people died from the disease. Treatment options are limited and relatively ineffective. Pancreatic cancer has a five-year survival rate of 1%–4% (Wolff et al., 2000), with 90% of patients succumbing to their disease within the first year of diagnosis (Rosenberg, 2000). Many comorbid conditions are associated with pancreatic cancer, including acute ascending cholangitis (AAC), a bacterial infection of the biliary tract that is caused by bile stasis secondary to obstruction.

Pathophysiology

Under normal circumstances, bile drains from the gallbladder to the duodenum via the common bile duct. In healthy people, several mechanisms are in place to prevent infection of the biliary system. The sphincter of Oddi prevents intestinal contents from refluxing into the common bile duct, the tight junctions between hepatocytes protect from transient bacteremia, and Kupffer cells maintain sterility of the biliary system with phagocytizing organisms (Sung, Costerton, & Shaffer, 1992). Additionally, bile has antibacterial properties of its own, including immunoglobulin A and bile salts (Sung et al.), and continuous flushing of biliary conduits occurs as bile flows from the liver to the intestine (Hanau & Steigbigel, 2000).

When the biliary system becomes obstructed, most commonly from bile duct stones, infection can occur. Jean Martin Charcot, MD, first described the relationship between common bile duct obstruction and sepsis in 1877. He described the triad of fever, jaundice, and right upper-quadrant pain, which later became known as Charcot’s triad (Lipsett & Pitt, 1990).

AAC is an infection of the biliary system in which bacteria present in the bile is unable to drain adequately because of an obstruction, stones, pancreatic cancer, or reflux of bile from the jejunum into the biliary system following a choledochojejunostomy (Hanau & Steigbigel, 2000). Duodenal microorganisms from the portal vein are thought to be the primary sources of biliary infection (Sung et al., 1992). Enteric flora are the most common organisms present. Aerobes constitute the majority of infections, with *E. coli* comprising 59% and *Klebsiella* causing 13.9% of the infections (Hanau & Steigbigel). Anaerobes are rare in biliary disease, but if present, bacterioides species and *Clostridia* organisms are the most common (Hanau & Steigbigel).

Anaerobes tend to be associated with more serious clinical illness than purely aerobic infections (Csendes et al., 1996; Shimada, Noro, Inamatsu, Urayama, & Adachi, 1981). Bile cultures are positive in 80%–100% of cases (Hanau & Steigbigel, 2000). Biliary infections are often polymicrobial (48%–61%), although blood cultures are usually positive for only one organism (Surawicz & Owen, 1995). Bacteremia occurs less frequently but is detected in 21%–83% of patients with cholangitis (Hanau & Steigbigel).

Since 1950, the etiology of AAC has shifted away from stone-induced disease to disease caused by obstruction by cancer (Lipsett & Pitt, 1990). This shift in etiology has been attributed, in part, to the use of long-term endoprostheses in patients with unresectable malignant tumors (Lipsett & Pitt). Endoprostheses, also known as endoscopic biliary stents or catheters, are used to decompress an obstructed biliary system. They are placed into the common bile duct to facilitate the drainage of bile into the jejunum, thereby relieving the pressure on the biliary system. The systemic toxicity that occurs in acute obstructive cholangitis results from entry of bacteria into the blood (Surawicz & Owen, 1995).

The primary infection mainly results from bacteria in the duodenum gaining entry and directly ascending into the biliary system, hence, ascending cholangitis (Surawicz & Owen, 1995). Increased intraductal pressure, as a result of the stricture, and bacterial growth lead to reflux of biliary contents and...
bacteremia (Hanau & Steigbigel, 2000; Rege, 1995). Anastomotic stricture formation can be caused by a variety of factors, including tension at the anastomosis, ischemia, and reflux of gastric and enteric contents into the biliary tree (Ammori, Joseph, Attia, & Lodge, 2000). Acute cholangitis can be life-threatening, and mortality may be as high as 100% for patients who develop hypotension, do not respond to conservative therapy, and do not receive timely drainage of bile (Hanau & Steigbigel). Early investigators found that mortality was higher for a first attack of cholangitis than for recurrent attacks (Boey & Way, 1980), and in a 1990 study by Deviere et al., the incidence of sepsisemia was significantly higher in cases of obstruction caused by cancer than in benign obstruction (21% versus 3%).

Patients with pancreatic cancer, particularly cancers located in the head of the pancreas, are likely to experience AAC at some point during their illness. Because impaired bile flow coupled with bacteria is essential in the development of cholangitis, many patients undergo choledochojunostomy or stent placement. Both of these procedures predispose patients to bile reflux and sludging. Biliary bacteria also can deconjugate bilirubin and hydrolyze phospholipids, which result in breakdown products that can form stones and sludge (Hanau & Steigbigel, 2000). This can lead to constricted bile ducts or obstructed catheters and stents. Direct ascension of bacteria from the duodenum is supported indirectly as a route of infection by occasional episodes of cholangitis in patients with surgically altered biliary drainage (Surawicz & Owen, 1995). Cholangitis is not produced by infected bile without obstruction or by obstruction without infected bile; both must be present for cholangitis to occur (Lipsett & Pitt, 1990).

Clinical Presentation

Patients with ACC typically present with fever, jaundice, and right upper-quadrant abdominal pain. Most patients develop a fever that usually is greater than 38°C (100.4°F) (Lipsett & Pitt, 1990). Jaundice and abdominal pain occur in approximately 60%–70% of patients, respectively (Hanau & Steigbigel, 2000); however, one early report noted that 20% of patients had temperatures below 38.5°C and no visible jaundice and only 70% had the complete triad of signs and symptoms (Boey & Way, 1980). More recently, jaundice has been observed in only 67% of patients, which can be explained by the increasing incidence of patients with malignant obstruction and indwelling catheters (Lipsett & Pitt). Right upper-quadrant tenderness without diffuse peritoneal signs is found in as many as two-thirds of patients with ACC (Lipsett & Pitt). Pain is usually mild; however, severe pain or marked tenderness on examination should prompt consideration of an alternative diagnosis such as acute cholecystitis (Lipsett & Pitt). The diagnosis of cholangitis may be difficult because abdominal pain, fever, and chills are often nonspecific (Surawicz & Owen, 1995).

Laboratory values typically include leukocytosis, hyperbilirubinemia, and elevated alkaline phosphatase level (Hanau & Steigbigel; Mueller, vanSonnenberg, & Simeone, 1982). Transaminases frequently are elevated in cholangitis, and serum amylase levels are elevated in approximately one-third of patients with cholangitis (Lipsett & Pitt). Two case studies illustrating the presentations and treatment of ACC are described in Inset 1.

Diagnostic Tests

Advances in imaging of the biliary tract have facilitated prompt and efficient diagnosis of ACC, immediate treatment, and improved patient response. Traditionally, ultrasonography (US) and computed tomography (CT) scans have been the first diagnostic modalities used when patients present with abdominal pain and jaundice. Some reports indicate that US has increased sensitivity and specificity in detecting common bile duct stones and other causes of biliary obstruction, including malignant and benign lesions (Hanau & Steigbigel, 2000; Lokich, Kane, Harrison, & McDermott, 1987). CT usually is considered more accurate than US for determining the cause and level of obstruction; however, the limitation of CT in diagnosing common bile duct stones is that many stones are radiolucent (Hanau & Steigbigel; Pickuth, 2000). CT has limited use in diagnosing cholangitis because the findings that specifically suggest bile duct infection, such as increased attenuation resulting from the presence of pus, bile duct wall thickening, or gas, are usually not visible (Hanau & Steigbigel). However, the use of spiral CT improves biliary tract imaging by acquiring several overlapping images in a short time, allowing volumetric acquisition and enabling two- and three-dimensional images to be displayed (Sajjad, Oxtoby, West, & Deakin, 1999; Wyatt & Fishman, 1997). Spiral CT is an ideal method with which to evaluate patients with suspected biliary tract obstruction because it can determine the cause of the obstruction (Wyatt & Fishman).

Obtaining adequate biliary drainage is imperative to the prevention and treatment of cholangitis. Endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic cholangiography (PTC) often are used to determine the cause and site of biliary obstruction. ERCP is an interventional radiology procedure that involves using a flexible fiberoptic tube (endoscope) to locate the ampulla of vater and injecting contrast medium into it against the flow of bile and pancreatic juices (White, 1990). Radiographs then are taken to visualize the common bile and pancreatic ducts (White). PTC is another interventional procedure that percutaneously accesses and drains the bile ducts. These procedures not only provide drainage of the biliary system but also can allow placement of a stent or drain. ERCP, introduced in 1968 (McCune, Shorb, & Moscovitz, 1968), is usually the preferred method to achieve cholangiography, followed by percutaneous and intraoperative techniques (Cohen, Siegel, & Kasmin, 1996). ERCP is considered the gold standard for imaging the biliary tract (Hanau & Steigbigel, 2000).

Risks associated with ERCP can include cholangitis, sepsis, perforation, seeding of the bloodstream with biliary bacteria, pancreatitis, aspiration, and perforation (Hanau & Steigbigel, 2000; Niederau, Pohlmann, Lubke, & Thomas, 1994). In a study by Lal, Lane, and Wong (2003), the most common complications of ERCP were pancreatitis and hemorrhage (4.76% and 2.38%, respectively) with no severe complications or procedure-related mortality. In a study by Masci et al. (2001), pancreatitis occurred in 1.8% of patients, hemorrhage occurred in 1.13% of patients, and the overall mortality rate was 0.12%. The accuracy of PTC is 89%–100% (Hanau & Steigbigel; Mueller, vanSonnenberg, & Simeone, 1982). Minor complications of PTC include leakage of bile, pain, mild venous hemobilia, biloma formation, fever, chills, and transient hyperamylasemia; major complications include sepsis, significant venous hemobilia, and arterial hemobilia (Winick, Waybill, & Venbrux, 2001).

Magnetic resonance cholangiopancreatography (MRCP) visualizes the biliary system by taking advantage of the fact that fluid found in the biliary tree is hyperdense on T2-weighted images, and MRCP also has the ability to analyze images in two- and three-dimensional projections (Hanau & Steigbigel, 2000). MRCP is as accurate as ERCP in almost all diagnostic aspects of cholangiopancreatography, and the lack of side effects and reduced discomfort for patients explain MRCP’s increasing popularity (Schoff, 2001). The accuracy of MRCP in detecting abnormalities of the biliary tree varies by report, although most found the
**Inset 1. Case Studies**

**Case study 1:** Mr. B is a 57-year-old male who was diagnosed with pancreatic carcinoma in August 1998 during surgery, which required placement of a biliary stent to relieve obstruction. On cycle 1, day 7 of his weekly gemcitabine chemotherapy at a dose of 440 mg/m² and concurrent daily radiation, he presented to the clinic with abdominal pain, nausea, vomiting, rigors, and a temperature of 39°C (102.2°F). He denied diarrhea. Laboratory studies and blood cultures were drawn peripherally and via his double-lumen Groshong central venous catheter (CVC). Findings were white blood cells 4.8/mm³ (neutrophils 93%), hemoglobin 9.5 g/dl, hematocrit 29%, platelet count 170,000/mm³, alkaline phosphatase 297 u/l, alanine aminotransferase 301 u/l, aspartate aminotransferase 187 u/l, and bilirubin 5.6 mg/dl. Mr. B’s CVC site was without redness, tenderness, or drainage. A chest x-ray and abdominal x-rays were obtained. He was admitted with a presumptive diagnosis of acute ascending cholangitis and was started on ampicillin sodium/subactam sodium and gentamicin. Cycle 2 of gemcitabine was held; however, he continued to receive daily radiation therapy.

The following day, he underwent an endoscopic retrograde cholangiopancreatography with replacement of biliary stent. He experienced immediate improvement of his nausea, vomiting, and abdominal pain. Blood cultures returned positive for *Enterococcus* and *E. coli* sensitive to ampicillin sodium/subactam sodium and gentamicin. Mr. B had no further complications and was able to complete his chemotherapy and radiation regimen without incident.

**Case study 2:** Mr. H is a 53-year-old male who was diagnosed with adenocarcinoma of the pancreas in February 1999. He underwent cholecystectomy, choledochojejunostomy, and retrogastric jejunojostomy. After completing treatment with weekly gemcitabine and concurrent daily radiation, he arrived in the clinic complaining of fevers, chills, and “yellow skin.” He stated that three to four days prior, he had chills and felt hot. The following day, he felt tired and “washed out” but denied having a fever. The day prior to coming into the clinic his urine was very dark but had become much clearer. Mr. H denied abdominal pain, nausea, vomiting, and diarrhea. Computed tomography of the abdomen revealed air in the biliary tree, which was unchanged from his previous scan. Laboratory values included white blood cell count 8.65/mm³, hemoglobin 13.0 g/dl, hematocrit 39.3%, platelet count 148,000/mm³, alkaline phosphatase 351 u/l, alanine aminotransferase 145 u/l, aspartate aminotransferase 52 u/l, and bilirubin 3.4 mg/dl. He was started on ciprofloxacin with follow-up at home.

The patient experienced several similar episodes over the next several months. His alkaline phosphatase elevated to 1,600 u/l. He underwent a magnetic resonance cholangiopancreatography, which showed a stricture near the entry of the bile duct into the jejunum, and percutaneous transhepatic catheter placement was performed. Following this procedure, he had no further febrile episodes and his laboratory values returned to normal.

**Nursing Care**

The nursing care of patients with ACC includes monitoring vital signs (temperature, pulse, respiratory rate, and blood pressure) every 15 minutes until stable or returned to baseline. Orthostatic vital signs are beneficial to determine fluid status and can be an early indicator of impending hypotension. Any changes in vital signs such as an increase in pulse or a decrease in blood pressure should be reported immediately to the physician or advanced practice nurse because these could be early indicators of sepsis. Laboratory work generally includes a complete blood count and differential, liver functions, calcium, magnesium, albumin, and electrolytes.

Prothrombin time and partial thromboplastin time should be obtained to assess bleeding status in preparation for any invasive procedures that may be needed. Amylase and lipase should be included to rule out pancreatitis. Urinalysis and urine culture in addition to blood cultures are obtained peripherally as well as via any central venous access device. Chest and abdominal x-rays may be obtained as indicated. Patients should take nothing by mouth for possible MRCP and/or CT scanning of the abdomen.

If oral medications are prescribed, patients can take clear liquids; however, if nausea and vomiting are present, medications should be given via IV when possible. IV hydration may be indicated, especially when patients are orthostatic or unable to take fluids orally because of nausea and vomiting. Antiemetics, such as ondansetron or granisetron, should be administered as needed. Monitoring of intake and output is essential to maintain homeostasis. Commence antibiotics as ordered. If the cholangitic episode is transient and has occurred just prior to being seen, patients should be observed closely.

Although abdominal pain is usually mild (Lipsett & Pitt, 1990), symptomatic pain medications, if indicated, can be administered orally or via IV. Ursodiol, a bile acid, is a litholytic therapy that is administered at a dose of 8–10 mg/kg per day, divided into two to three doses. It may be started to avoid sensitivity of the procedure to be greater than 85% and specificity greater than 88% (Hanau & Steigbigel) (see Figure 1). Only very small stones, ampullary lesions, tiny fistulas, and air in bile ducts are difficult to visualize with MRCP (Schoff). In patients who are unable to undergo ERCP, such as those with choledochojejunostomies, MRCP is often the diagnostic test of choice.
Acute Ascending Cholangitis

- Acute ascending cholangitis (AAC) is an infection of the biliary system in which bacteria present in the bile is unable to drain adequately because of obstruction, commonly caused by stones, pancreatic cancer, or reflux of bile from the jejunum into the biliary system following a choledochojejunostomy.
- Patients with pancreatic cancer, particularly cancer in the head of the pancreas, are likely to experience AAC at some point during their illness.
- The severity of the clinical course is dependent on the extent of the obstruction and the virulence of the organism.
- Charcot’s triad (fever, jaundice, and right upper-quadrant abdominal pain) is a common presentation of AAC.
- Enteric flora are the most common organisms causing cholangitis.
- Survival depends on early recognition of the syndrome, immediate adequate drainage of the biliary system, and intensive medical therapy.