79

Neoplasms of the Gallbladder and Biliary Tract

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CHAPTER OUTLINE

Most neoplasms that arise from the gallbladder and bile ducts are malignant. Although infrequent, gallbladder and bile duct carcinomas are not rare. Gallbladder carcinoma is the seventh most common malignant neoplasm of the gastrointestinal tract and the most common biliary malignant neoplasm; bile duct carcinoma occurs less often.[1] Familiarity with the imaging characteristics of gallbladder and bile duct neoplasms is important to expedite diagnosis and appropriate treatment of patients, who often present with nonspecific symptoms of right upper quadrant pain, jaundice, and weight loss.

Gallbladder Carcinoma

EPIDEMIOLOGY

Carcinoma of the gallbladder is responsible for at least 3000 deaths per year in the United States.[1] Gallbladder cancer is the sixth most common cancer of the digestive system but accounts for only 3% to 4% of all gastrointestinal cancers. Carcinoma of the gallbladder is two to three times more common in women than in men, and its incidence steadily increases with age, although it varies greatly in different parts of the world.[2-6] More than 90% of patients are older than 50 years; the peak incidence is 70 to 75 years. Some geographic areas have a high incidence of gallbladder cancer, including South America and India.[5] Certain groups, such as Israelis, Native Americans, Spanish Americans in the southwest United States, and Eskimos in Alaska, have a significantly higher incidence of gallbladder carcinoma and cholelithiasis than do populations.[7,8]

ETIOLOGY

Several factors have been associated with an increased risk for development of gallbladder carcinoma. The presence of gallstones is considered to be an important risk factor for gallbladder carcinoma. Of patients with gallbladder carcinoma, 65% to 90% have gallstones, an incidence considerably higher than that for age- and sex-matched control groups.[6,9] Many gallbladder cancers are unsuspected and found incidentally during surgery for gallstones or on final histologic analysis of the specimen. Diffuse mural calcification, the "porcelain" gallbladder, is another predisposing factor, ranging from 20% to 50% leading to cancer.[10,11] Other risk factors include the presence of gallbladder adenomas, an anomalous pancreaticobiliary duct junction, and exposure to carcinogenic chemicals.[6,12,13]

PATHOLOGIC FINDINGS

Most carcinomas of the gallbladder are adenocarcinomas (85%-90%) and can be papillary, tubular, mucinous, or signet cell type. The remainder are anaplastic, squamous cell, or adenosquamous carcinomas.[14,15] On macroscopic examination, carcinomas of the gallbladder can appear as poorly defined areas of diffuse gallbladder wall thickening (infiltrating), often with a desmoplastic reaction, or as a cauliflower mass (fungating) that grows into the gallbladder lumen. The infiltrating type invades the gallbladder wall and ultimately replaces the lumen with a tumor mass. The papillary form grows into and eventually fills the lumen.[16] Some tumors may show a combination of the infiltrating and fungating patterns. Approximately 60% of carcinomas originate in the fundus, 30% in the body, and 10% in the neck.[17] In some cases, the tumor may diffusely infiltrate the entire gallbladder, making its organ of origin impossible to identify.

The gallbladder has unique anatomic features; the wall consists of a mucosa, lamina propria, smooth muscle layer, perimuscular connective tissue, and serosa without a submucosa. Furthermore, no serosa exists at the attachment to the liver and along the hepatic surface. The connective tissue is continuous with the interlobular connective tissue of the liver.[17] Gallbladder carcinoma is staged surgically by the depth of invasion, extension of disease into adjacent structures, involvement of lymph nodes, and presence of metastases by the American Joint Committee on Cancer TNM staging system[2,18]

BOX 79-1 TNM CLASSIFICATION SYSTEM FOR STAGING GALLBLADDER CARCINOMA

PRIMARY TUMOR (T)

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor invades mucosa or muscle layer
T1a	Tumor invades the mucosa
T1b	Tumor invades the muscle layer
T2	Tumor invades the perimuscular connective tissue; no extension beyond the serosa or into the liver
T3	Tumor perforates the serosa (visceral peritoneum) and/or directly invades the liver and/or one other adjacent organ or structure such as stomach, duodenum, colon, pancreas, omentum, or extrahepatic bile ducts
T4	Tumor invades main portal vein or hepatic artery or invades two or more extrahepatic organs or structures

REGIONAL LYMPH NODES (N)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastases to nodes along the cystic duct, common bile duct, hepatic artery, and/or portal vein
N2	Metastases to periaortic, pericaval, superior mesenteric artery and/or celiac artery lymph nodes

DISTANT METASTASIS (M)

M0	No distant metastasis
M1	Distant metastasis

STAGE GROUPING

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3	N0	M0
Stage IIIB	T1-3	N1	M0
Stage IVA	T4	N0-1	M0
Stage IVB	Any T	N2	M0
	Any T	Any N	M1

From Edge SB, Byrd DR, Compton CC, et al (eds): AJCC Cancer Staging Manual, 7th ed. Chicago, Springer, 2010, pp 211–217.

(Box 79-1). Invasion of the muscularis mucosa distinguishes T1 from T2 cancers.

CLINICAL FINDINGS

Gallbladder carcinoma most often is manifested with right upper quadrant abdominal pain simulating more common biliary and nonbiliary disorders.[19] Weight loss, jaundice, and an abdominal mass are less common presenting symptoms. Patients may have long-standing symptoms of chronic cholecystitis with a recent change in the quality or frequency of the painful episodes. Other common presentations are similar to either acute cholecystitis or symptoms of biliary malignant disease. Hepatomegaly and ascites suggest liver invasion. Gallbladder carcinoma is occasionally an incidental finding on abdominal imaging studies. Elevated serum levels of α-fetoprotein and carcinoembryonic antigen have been reported in association with gallbladder carcinoma.[17,20]

RADIOGRAPHIC FINDINGS

Traditional plain oral cholecystography and barium studies of the gastrointestinal tract have a limited role in the imaging of gallbladder carcinoma. Abdominal radiographs may show calcified gallstones, porcelain gallbladder, or, rarely, punctate calcifications from mucinous carcinomas.[21] Biliary gas from malignant gallbladder–enteric fistula is another rare finding.[22] The gallbladder fails to opacify in at least two thirds of patients with carcinoma of the gallbladder, usually because of cystic duct obstruction.[16] Barium study findings are abnormal in limited cases, showing displacement or direct invasion of the duodenum or anterior limb of the hepatic flexure.

Ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) are the most valuable imaging modalities for evaluation of patients with gallbladder carcinoma. Patients with right upper quadrant pain should initially be examined with ultrasound. Ultrasound can detect lesions suggestive of gallbladder cancer, such as a wide polyp base and irregular borders. The diagnostic accuracy of ultrasound in gallbladder cancer is more than 80%, but it has limitations in tumor staging.[23] Ultrasound can be useful for differentiating adenomyomatosis from the wall-thickening type of gallbladder cancer by detecting intramural cystic spaces or echogenic foci within the wall.[24-28] Doppler imaging can be useful for differentiating polyp from tumefactive sludge by demonstrating blood flow to the polypoid tumors (Fig. 79-1). Endoscopic ultrasound is useful in depicting the depth of tumor invasion and for characterizing polypoid lesions.[26,27] CT is superior to ultrasound in assessing lymphadenopathy and spread of the disease into the liver, porta hepatis, or adjacent structures and is useful in predicting which patients will benefit from surgical therapy (Fig. 79-2).[28,29] Although MRI can be useful in assessing the cause of focal or diffuse mural thickening and helps differentiate gallbladder cancer from adenomyomatosis and chronic cholecystitis,[30,31] magnetic resonance cholangiopancreatography (MRCP) provides more detailed information than ultrasound or CT about biliary involvement of the tumor. In addition, adding diffusion-weighted imaging to the standard MRI protocol may improve sensitivity for distinguishing gallbladder cancers from benign gallbladder diseases with wall thickening (Fig. 79-3).[32-34] Although direct cholangiographic techniques such as endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic cholangiography are of little value in detecting the presence of gallbladder carcinoma, they are helpful in planning the surgical procedure because they can show tumor growth into adjacent intrahepatic ducts or into the common bile duct.[6] The cholangiographic differential diagnosis includes cholangiocarcinoma, metastases, Mirizzi syndrome, and pancreatic carcinoma.

Radiologic Evaluation of the Primary Tumor

Gallbladder carcinomas have three major histologic and imaging presentations: focal or diffuse thickening or irregularity of the gallbladder wall; polypoid mass originating in the gallbladder wall and projecting into the lumen; and most commonly, a mass obscuring or replacing the gallbladder, often invading the adjacent liver.[25,28,30]

Carcinoma Manifesting as Mural Thickening. Focal or diffuse thickening of the gallbladder wall is the least common presentation of gallbladder carcinoma and is the most difficult to diagnose, particularly in the early stages. Gallbladder carcinoma may cause mild to marked mural thickening in a focal or diffuse pattern. This thickening is best appreciated sonographically; the gallbladder wall is normally 3 mm or less in

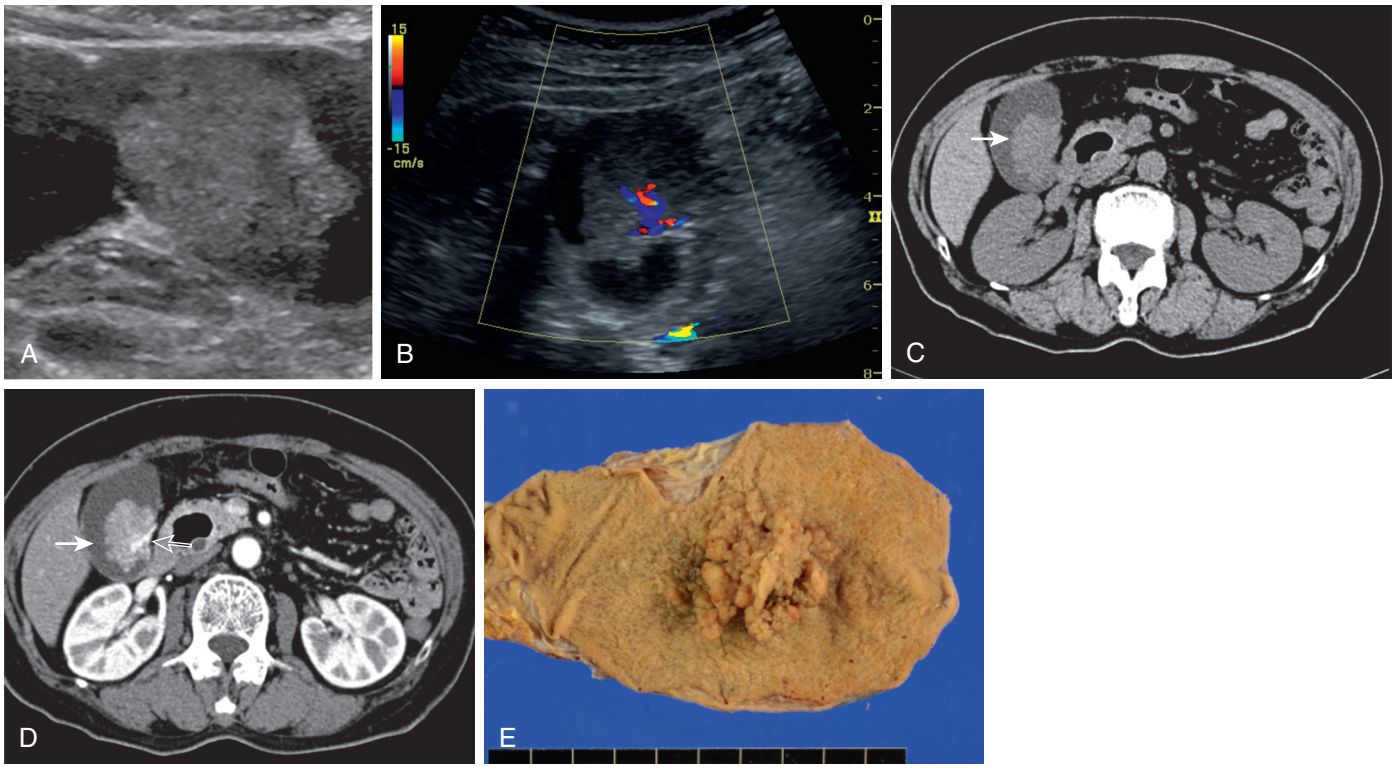

Figure 79-1 Ultrasound and Color Doppler imaging findings of polypoid gallbladder carcinoma. A. Subcostal sonogram shows a polypoid mass with a homogeneous tissue texture that is fixed to the gallbladder wall at its base. **B.** Color Doppler imaging shows blood flow signals in the polypoid mass. **C.** Precontrast axial CT scan demonstrates a polypoid mass (*arrow*) showing hyperattenuation to surrounding bile of the gallbladder. **D.** Axial CT scan demonstrates a homogeneously enhancing polypoid gallbladder carcinoma (*arrow*) with an enhancing vessel (*open arrow*). **E.** Photograph of the opened resected specimen shows the cauliflower-like intraluminal growth of a papillary adenocarcinoma.

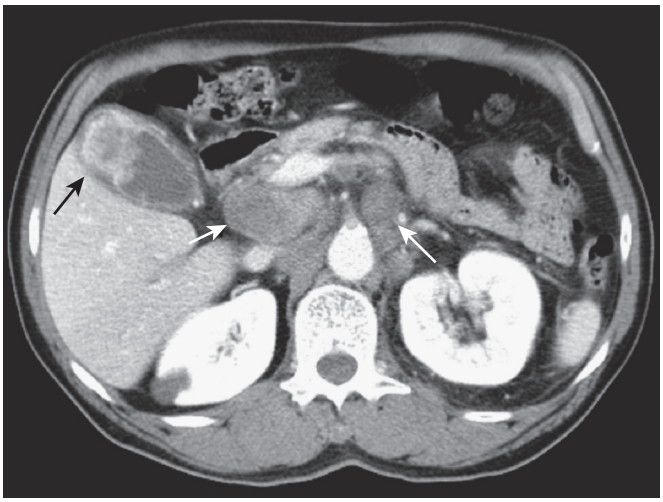

Figure 79-2 Polypoid gallbladder carcinoma with nodal metastasis. CT scan demonstrates a polypoid gallbladder carcinoma (*black arrow*) and low-density portocaval and para-aortic lymph nodes containing metastases (*white arrows*).

thickness.[35] Carcinomas confined to the gallbladder mucosa may be manifested as flat or slightly raised lesions with mucosal irregularity that are difficult to appreciate sonographically. In one sonographic series, half the patients with these early carcinomas had no protruding lesions, and fewer than one third were identified preoperatively.[36] More advanced gallbladder carcinomas can cause marked mural thickening, often with irregular and mixed echogenicity (Fig. 79-4). The gallbladder may be contracted, normal sized, or distended, and gallstones are usually present. When cancer occurs in the neck portion of the gallbladder, identification of cystic duct involvement by the tumor on imaging merits consideration of focal bile duct resection to achieve a negative resection margin (see Fig. 79-4).

Four factors interfere with the sonographic recognition of carcinoma as the cause of gallbladder wall thickening:

1. Changes of early gallbladder carcinoma may be only subtle mucosal irregularity or mural thickening.
2. Gallbladder wall thickening is a nonspecific finding that can also be caused by acute or chronic cholecystitis, hyperalimentation, portal hypertension, adenomyomatosis, inadequate gallbladder distention, hypoalbuminemia, hepatitis, hepatic failure, cardiac failure, or renal failure. The echo architecture of the wall can sometimes help narrow the differential diagnosis.[37,38] In acute cholecystitis, the wall often has irregular, discontinuous hypoechoic and echogenic bands. Chronic cholecystitis often results in a uniformly echodense band surrounding the mucosa, and hypoproteinemia may have a hypoechoic central band. Pronounced wall thickening (>1.0 cm) demonstrated by ultrasonography with associated mucosal irregularity or marked asymmetry should raise concerns for malignant disease or complicated cholecystitis.[24,25]
3. Chronic cholecystitis is often present in patients with gallbladder carcinoma.
4. Shadowing stones or gallbladder wall calcification may obscure the carcinoma.

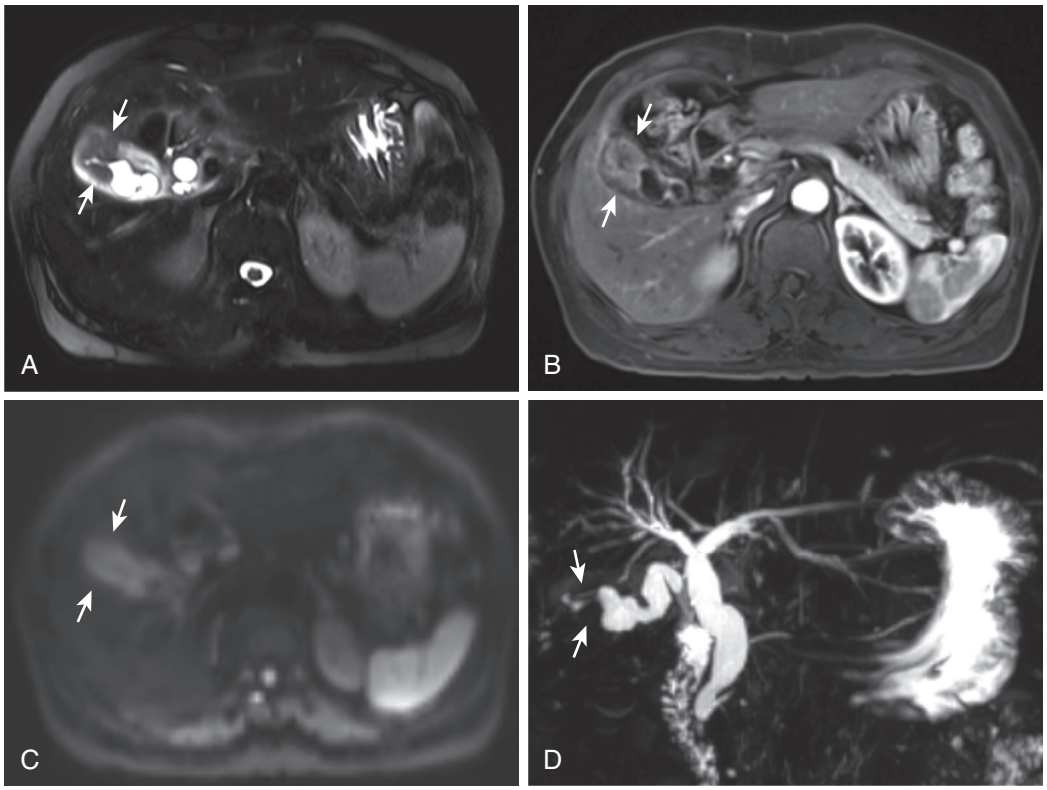

Figure 79-3 Gallbladder cancer showing enhancement on MRI and a high signal intensity on diffusion-weighted imaging. A. Fat-suppressed T2-weighted MR image shows an asymmetrically thickened gallbladder wall with hypointensity (*arrows*) compared with edematous surrounding wall. **B.** Postgadolinium fat-suppressed T1-weighted image reveals slightly heterogeneous enhancement of the thickened gallbladder wall (*arrows*). **C.** High b value (b = 1000) diffusion-weighted imaging demonstrates a high signal intensity of the tumor (*arrows*) involving the fundus of the gallbladder. **D.** MRCP demonstrates a luminal narrowing of the fundus (*arrows*) caused by the tumor and a normal appearance of the bile duct.

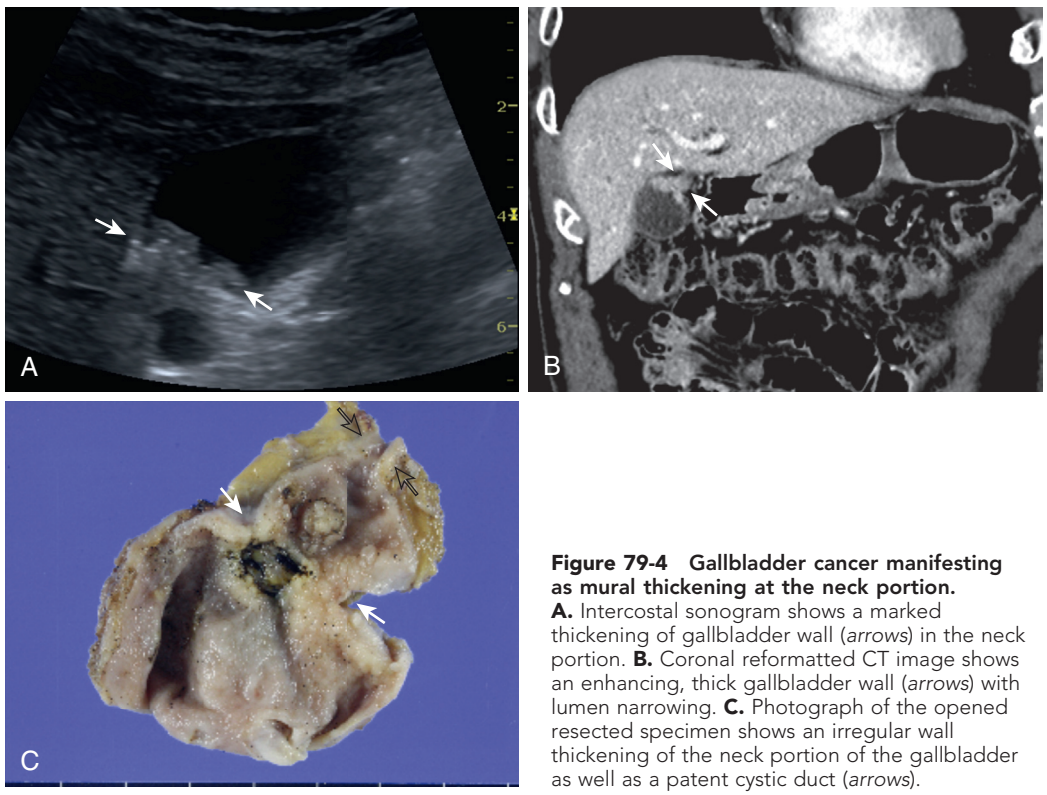

Figure 79-4 Gallbladder cancer manifesting as mural thickening at the neck portion. A. Intercostal sonogram shows a marked thickening of gallbladder wall (*arrows*) in the neck portion. **B.** Coronal reformatted CT image shows an enhancing, thick gallbladder wall (*arrows*) with lumen narrowing. **C.** Photograph of the opened resected specimen shows an irregular wall thickening of the neck portion of the gallbladder as well as a patent cystic duct (*arrows*).

Although CT is inferior to ultrasound for evaluating the gallbladder wall for mucosal irregularity, mural thickening, and cholelithiasis, it is superior for evaluating the thickness of portions of the gallbladder wall that are obscured by interposed gallstones or mural calcifications on ultrasound.[28,37,39] On contrast-enhanced CT, thick (>2.5 mm) and strong enhancement of the inner wall and irregular contour of the affected wall are significant predictors for a malignant cause of gallbladder wall thickening (Fig. 79-5).[29,40] When focal or irregular thickening of the gallbladder wall is encountered on CT, the images should be carefully inspected for bile duct dilation, local invasion, metastasis, or adenopathy.[29,40] Multiplanar reformatted images of multidetector CT (MDCT) scans could be valuable for demonstrating extent of gallbladder cancers as well as relationship with adjacent organs, similar to biliary malignant tumors[41-44] (see Fig. 79-4). Studies have also demonstrated that diffusion-weighted MRI could contribute to the improvement of the diagnostic capability for gallbladder wall thickening or polypoid lesions by demonstrating high signal intensity on high b value diffusion-weighted imaging and a lower apparent diffusion coefficient value of gallbladder cancers than that of benign gallbladder diseases (see Fig. 79-3).[32,33]

Carcinoma Manifesting as a Polypoid Mass. About one fourth of gallbladder carcinomas are manifested as a polypoid mass projecting into the gallbladder lumen. Identification of these neoplasms is particularly important because they are well differentiated and are more likely to be confined to the gallbladder mucosa or muscularis when discovered.[36,45]

Polypoid carcinomas on ultrasound usually have a homogeneous tissue texture, are fixed to the gallbladder wall at their base, and do not cast an acoustic shadow[25,27] (Fig. 79-6; see also Fig. 79-1). Most are broad based with smooth borders, although occasional tumors have a narrow stalk or villous fronds. The polyp may be hyperechoic, hypoechoic, or isoechoic relative to the liver. Gallstones are usually present, and the gallbladder is either normal sized or expanded by the mass. A small polypoid carcinoma can be indistinguishable from a cholesterol polyp, adenoma, or adherent stone. Most benign polyps are small, measuring less than 1 cm.[26,27,37] If a gallbladder polyp is larger than 1 cm in diameter and is not clearly benign, cholecystectomy should be considered.[36] Tumefactive sludge or blood clot can simulate a polypoid carcinoma.[25] Positional maneuvers usually differentiate these entities; clots and sludge move, albeit slowly, whereas cancers do not. Color Doppler imaging is also valuable for differentiating a polypoid tumor from tumefactive sludge by demonstrating vascular flow within tumors[28] (see Fig. 79-1). When polypoid carcinomas are sufficiently large, they are manifested as soft tissue masses that are denser than surrounding bile on CT scans or show a hypointensity to surrounding bile on T2-weighted MR imaging (see Fig. 79-6).[30] The polypoid cancer usually enhances homogeneously after administration of contrast medium, and the adjacent gallbladder wall may be thickened (see Figs. 79-1 and 79-6). Necrosis or calcification is uncommon.

Carcinoma Manifesting as a Gallbladder Fossa Mass. A large mass obscuring or replacing the gallbladder is the most common (42%-70%) presentation of gallbladder carcinoma.[28,30] On sonographic examination, the mass is often complex, with regions of necrosis, and small amounts of pericholecystic fluid are often present. Gallstones are commonly seen within the ill-defined mass, which typically invades hepatic parenchyma.

On CT scans, infiltrating carcinomas that replace the gallbladder often show irregular contrast enhancement with scattered regions of internal necrosis (Fig. 79-7).[30] Unless the associated gallstones are densely calcified, they may be difficult to identify. Invasion of the liver or hepatoduodenal ligament,

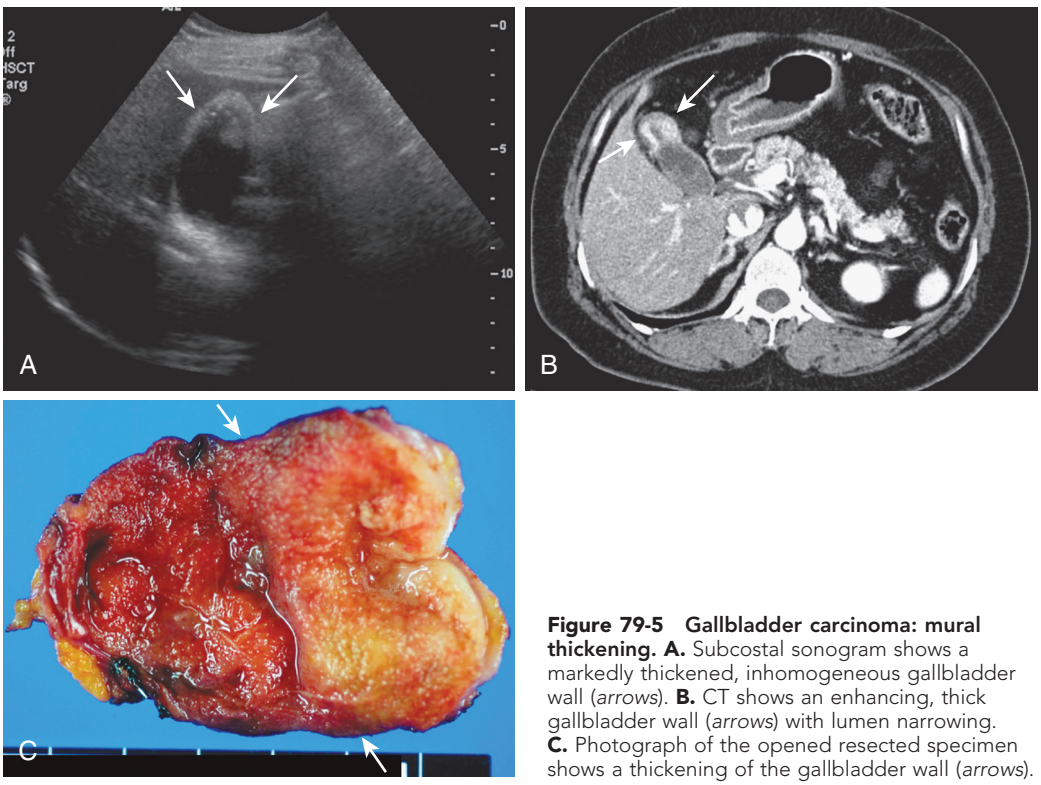

Figure 79-5 Gallbladder carcinoma: mural thickening. A. Subcostal sonogram shows a markedly thickened, inhomogeneous gallbladder wall (*arrows*). **B.** CT shows an enhancing, thick gallbladder wall (*arrows*) with lumen narrowing. **C.** Photograph of the opened resected specimen shows a thickening of the gallbladder wall (*arrows*).

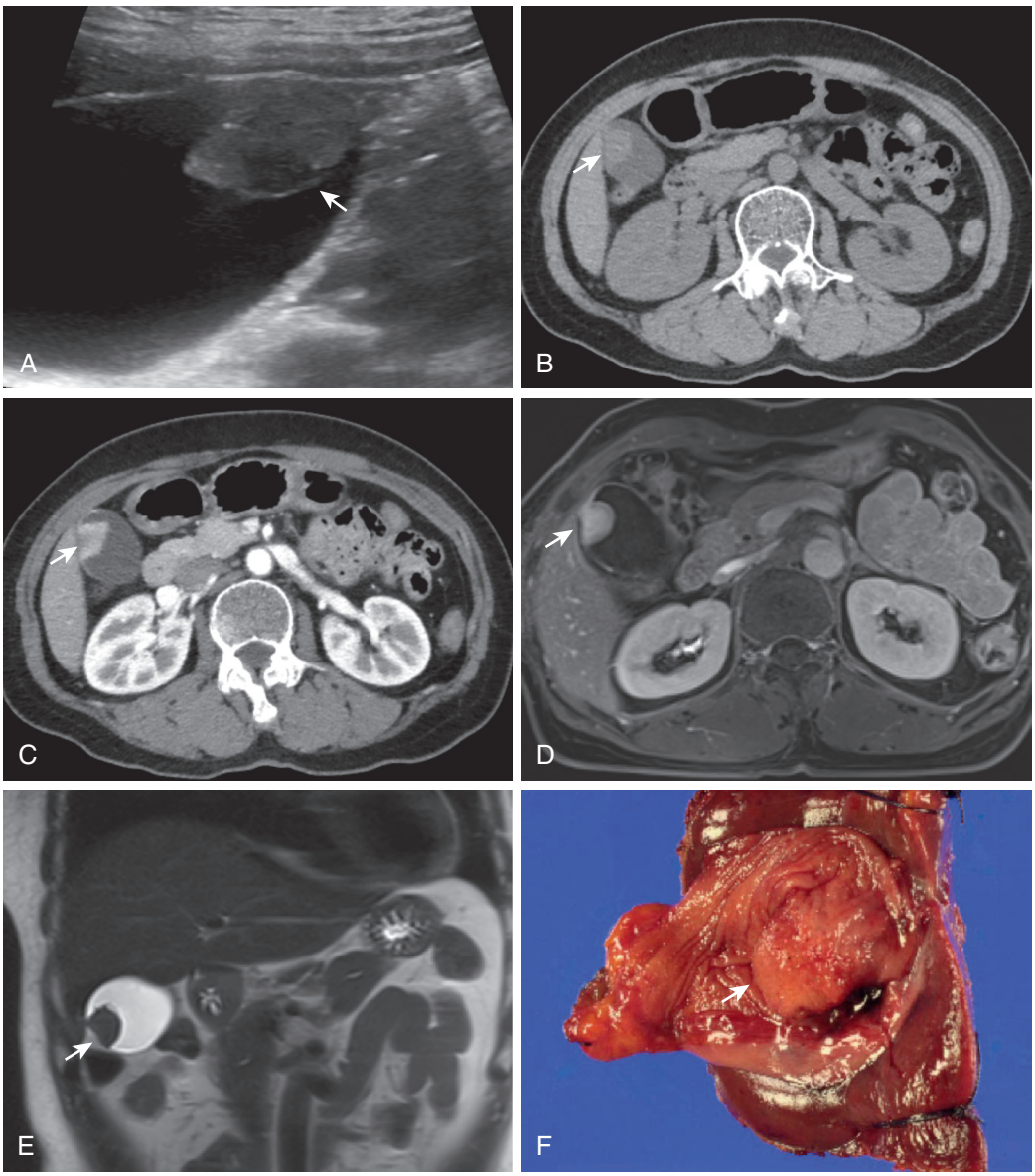

Figure 79-6 Polypoid gallbladder carcinoma having a wide base with a gallbladder wall. A. Sonogram shows a large homogeneous, hyperechoic polypoid gallbladder carcinoma (*arrow*) relative to surrounding bile. The mass was immobile with changes in the patient's position. **B.** Precontrast axial CT scan demonstrates a hyperattenuated soft tissue density polypoid tumor (*arrow*) in the gallbladder. **C.** Postcontrast axial CT scan demonstrates a homogeneously enhancing polypoid gallbladder carcinoma that is broad based with smooth border (*arrow*). **D.** Postcontrast T1-weighted MR image also demonstrates a polypoid mass showing hyperenhancement (*arrow*). **E.** Coronal T2-weighted image demonstrates a hypointense polypoid tumor (*arrow*) in the gallbladder. **F.** Photograph of the opened resected specimen shows a polypoid gallbladder cancer (*arrow*).

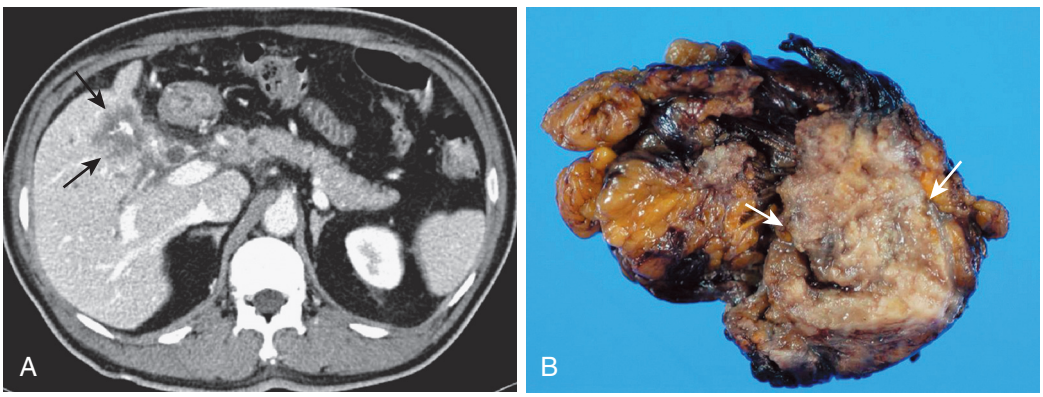

Figure 79-7 Gallbladder carcinoma manifesting as a gallbladder fossa mass. A. CT scan demonstrates an irregular hypodense mass replacing the gallbladder extending into the hepatic parenchyma (*arrows*). Note dilated common duct with wall thickening, suggesting spreading to the extrahepatic bile duct. **B.** Photograph of the resected specimen shows a large mass replacing the gallbladder (*arrows*).

satellite lesions, hepatic or nodal metastases, and bile duct dilation are also common.

MRI findings in gallbladder carcinoma are similar to those reported with CT. MRI demonstrates prolongation of the T1 and T2 relaxation time in gallbladder carcinoma. These lesions are heterogeneously hyperintense on T2-weighted images and hypointense on T1-weighted images compared with liver parenchyma.[46] Ill-defined early enhancement is a typical appearance of gallbladder carcinoma on dynamic gadolinium-enhanced MRI[29] (Fig. 79-8). MRI with MRCP offers the potential of evaluating parenchymal, vascular, biliary, and nodal involvement with a single noninvasive examination (Fig. 79-9).[30] On the basis of MRI alone, it may be difficult to distinguish carcinoma of the gallbladder from inflammatory and metastatic disease.

Differential Diagnosis

The differential diagnosis of infiltrating gallbladder carcinomas includes more common inflammatory and noninflammatory causes of wall thickening. These include heart failure, cirrhosis, hepatitis, renal failure, complicated cholecystitis, xanthogranulomatous cholecystitis, and adenomyomatosis.[28,38,39] Clinically and radiologically, gallbladder carcinoma can be difficult to differentiate from cholecystitis with pericholecystic fluid and abscess. A increased attenuation intrahepatic halo surrounding the gallbladder wall on contrast-enhanced CT scans or MRI is fairly specific for complicated cholecystitis.[46,47,48] Gallbladder carcinoma should be suspected when there are features of a focal mass, lymphadenopathy, hepatic metastases, and biliary obstruction at the level of the porta hepatis. Diffuse gallbladder wall thickening and streaky densities in the pericholecystic fat are seen with both inflammation and carcinoma.[40] Xanthogranulomatous cholecystitis is a pseudotumoral inflammatory condition of the gallbladder that radiologically simulates gallbladder carcinoma.[49] In the few cases in which it is impossible to distinguish complicated cholecystitis from neoplasm, ultrasound-directed or CT-directed needle biopsy can provide a tissue diagnosis. Adenomyomatosis, which is characterized by focal or diffuse gallbladder wall thickening with dilated Rokitansky-Aschoff sinuses, may simulate gallbladder carcinoma on CT. MRI can be useful for distinguishing this entity from gallbladder carcinoma.[30,31]

The differential diagnosis of those tumors that are manifested as an intraluminal polypoid mass includes adenomatous, hyperplastic, and cholesterol polyps; carcinoid tumor; metastatic melanoma; and hematoma.[28] The differential diagnosis for a mass replacing the gallbladder fossa includes hepatocellular carcinoma, cholangiocarcinoma, and metastatic disease to the gallbladder fossa.[30] Hepatomas occurring near the gallbladder fossa may be confused with gallbladder cancer radiographically, but they usually occur in cirrhotic livers and do not typically invade the gallbladder. Patients with liver metastases to the gallbladder fossa usually have a known primary neoplasm.

Pathways of Tumor Spread

Gallbladder carcinoma spreads beyond the wall by several routes: direct invasion of the liver, hepatoduodenal ligament, duodenum, or colon; lymphatic spread to regional lymph nodes; hematogenous spread to the liver; intraductal tumor extension; and metastasis to the peritoneum.[50,51] Distant metastases are unusual.

Gallbladder carcinoma spreads most commonly by direct invasion of the liver.[50-52] Liver invasion is facilitated by its proximity and the thin gallbladder wall, which lacks a submucosa and has only a single muscle layer. Invasion of the gastrohepatic

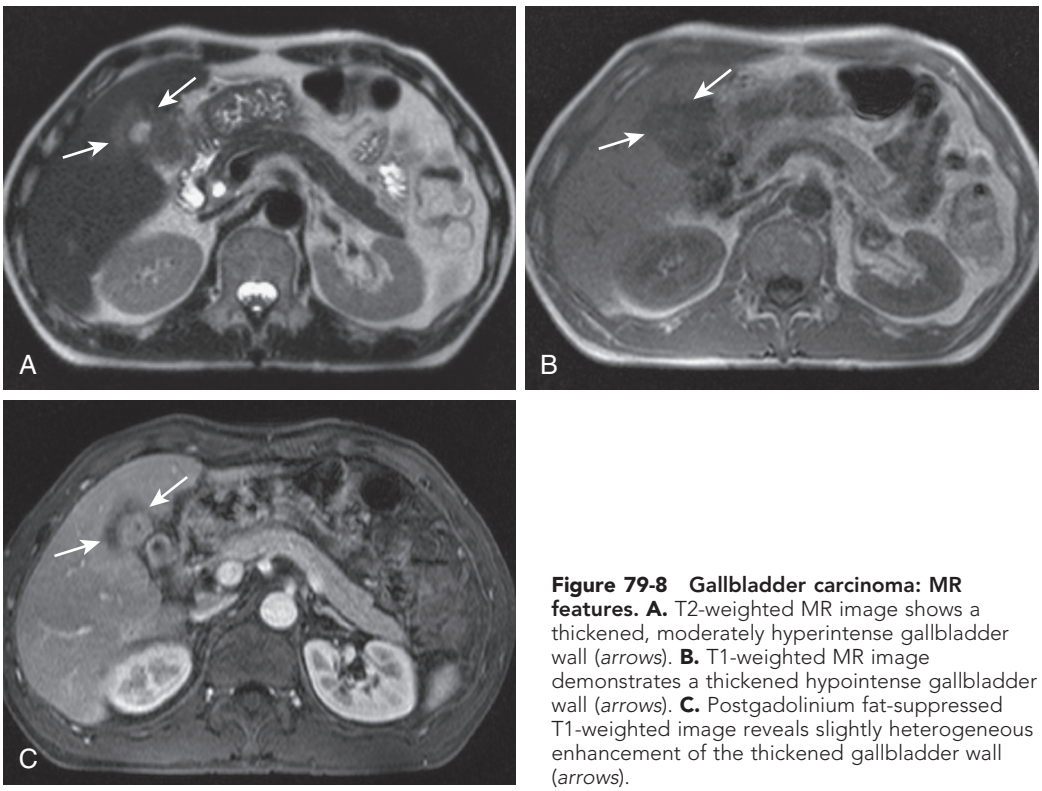

Figure 79-8 Gallbladder carcinoma: MR features. A. T2-weighted MR image shows a thickened, moderately hyperintense gallbladder wall (*arrows*). **B.** T1-weighted MR image demonstrates a thickened hypointense gallbladder wall (*arrows*). **C.** Postgadolinium fat-suppressed T1-weighted image reveals slightly heterogeneous enhancement of the thickened gallbladder wall (*arrows*).

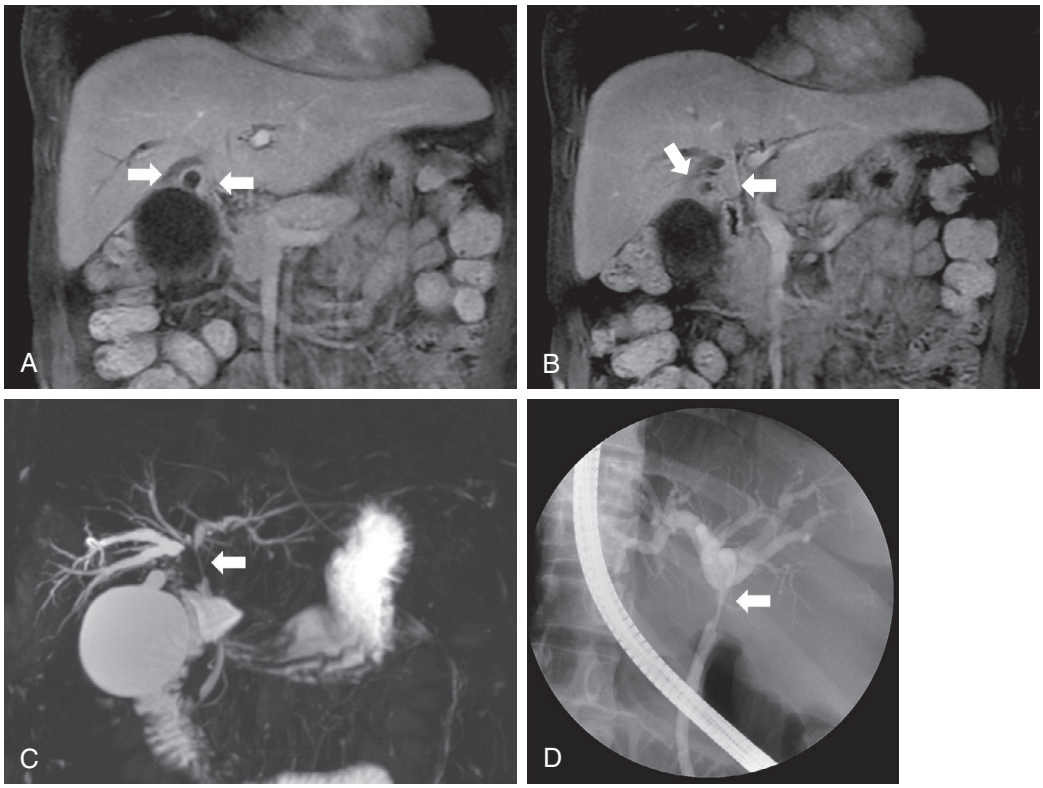

Figure 79-9 Gallbladder carcinoma with direct spread to the bile duct. A and **B.** Coronal MR images demonstrate an enhancing gallbladder carcinoma with involvement of adjacent bile duct (*arrows*). **C.** MRCP maximum intensity projection image demonstrates a malignant stricture involving the common hepatic duct as well as narrowing of the lumen at neck portion of the gallbladder (*arrow*). **D.** Direct cholangiography also demonstrates the stricture (*arrow*) involving the confluence of the right and left hepatic ducts (hilum of the bile duct), with dilation of the intrahepatic bile ducts.

ligament is also common and may cause biliary obstruction at the porta hepatis. Invasion into the duodenum or colon is less common. On ultrasound images, the gallbladder wall becomes ill-defined as an inhomogeneous mass extends into the liver parenchyma. On CT scans, portions of the invading tumor show enhancement after administration of contrast medium.[53] The gallbladder wall is poorly defined adjacent to the carcinoma invading liver parenchyma. Detection of subtle hepatic invasion is improved by use of narrow collimation to avoid partial volume averaging and by coronal or sagittal reformations.[54] On MRI, direct hepatic invasion and distant liver metastases are well shown on T2-weighted or gadolinium-enhanced images. The tumor has the same signal intensity as the primary tumor in most cases.[30]

The prevalence of lymphatic spread is high in gallbladder carcinoma[55] (see Fig. 79-2). Lymphatic metastases progress from the gallbladder fossa through the hepatoduodenal ligament to nodal stations near the head of the pancreas. The cystic and pericholedochal lymph nodes are the most commonly involved at surgery and are a critical pathway to involvement of the celiac, superior mesenteric, and para-aortic lymph nodes.[52-55] Because the gallbladder drains into these more distal nodes, hepatic hilar nodes are usually not involved. Positive lymph nodes are more likely to be greater than 10 mm in anteroposterior diameter and have heterogeneous contrast material enhancement.[53,54]

Dilated bile ducts are present in about half the patients at the time of presentation.[28,53,54] Biliary obstruction may develop in patients with gallbladder cancer for a variety of reasons: lymphadenopathy, usually surrounding the common bile duct; tumor invasion into the hepatoduodenal ligament, often at the porta hepatis (see Fig. 79-9); intraductal tumor growth; or rarely, choledocholithiasis. Adenopathy and invasion into the hepatoduodenal ligament are the most common causes of obstruction; intraductal spread is infrequent but may be seen as a polypoid mass extending into the common bile duct. Ultrasound, CT, and MRI reveal biliary dilation and can usually show the level of obstruction. Invasion of the hepatoduodenal ligament is often better demonstrated with coronal reformatted CT or MRI than with axial CT.[56-58]

TREATMENT AND PROGNOSIS

Survival in patients with gallbladder carcinoma is strongly influenced by the pathologic stage at presentation.[16,59] Patients with cancer limited to the gallbladder mucosa have an excellent prognosis, but most patients with gallbladder carcinoma have advanced, unresectable disease at the time of presentation. As a result, less than 15% of all patients with gallbladder carcinoma are alive after 5 years. Surgical management of gallbladder carcinoma is based on the local extension of the tumor. If there is direct extension of disease to the muscularis propria, a radical cholecystectomy is necessary. When disease extends through the serosa, more radical procedures including extended cholecystectomy, pancreatoduodenectomy, and major hepatic resection can be performed. However, radical tumor resection in this

setting is associated with a high operative mortality and few long-term survivors.

Other Malignant Gallbladder Neoplasms

A number of malignant diseases can metastasize to the gallbladder. Among the most common primary malignant neoplasms are melanoma, breast carcinoma, hepatocellular carcinoma, and lymphoma.[57,60-62] On cross-sectional images, metastases show focal wall thickening, one or more polypoid masses, or replacement of the gallbladder by neoplasm (Fig. 79-10). Metastatic neoplasms of the gallbladder may be indistinguishable from primary gallbladder carcinoma except that gallstones are less frequently seen in patients with metastases.

Primary carcinoid tumors, lymphomas, and sarcomas of the gallbladder have also been reported.[16,54] Carcinoids and lymphomas are manifested as polypoid masses that sometimes obstruct the cystic duct.[63] Sarcomas are bulky polypoid masses that are indistinguishable from primary gallbladder carcinoma.

Benign Gallbladder Neoplasms

A diverse spectrum of benign tumors arise from the gallbladder. Benign neoplasms are derived from the epithelial and nonepithelial structures that compose the normal gallbladder.[64] Although these lesions are relatively uncommon, their importance lies in their ability to mimic malignant lesions of the gallbladder. Most benign neoplasms of the gallbladder are adenomas. At gross examination, gallbladder adenomas appear as polypoid structures and may be sessile or pedunculated. They are generally smaller than 2 cm. Tubular adenomas are typically lobular in contour, whereas papillary adenomas have a cauliflower-like appearance.[64]

On ultrasound, adenomas appear as small, broad-based, nonshadowing, sessile or pedunculated polypoid filling defects that do not move with gravitational maneuvers. The echotexture of adenomas is typically homogeneous and hyperechoic. Adenomas tend to be less echogenic and more heterogeneous as they increase in size[64] (Fig. 79-11). Focal gallbladder wall thickening adjacent to a polypoid mass should raise concern for malignant disease. These polyps are manifested as enhancing intraluminal soft tissue masses. They are difficult to distinguish from the more common cholesterol polyp. Cholesterol polyps are more often smaller and multiple. Other rare benign neoplasms of the gallbladder include cystadenoma, granular cell tumors, hemangioma, lipoma, and leiomyoma.[64-66]

Cholangiocarcinoma

EPIDEMIOLOGY

Cholangiocarcinoma is a malignant tumor arising from the epithelium of the bile ducts and is the second most common primary hepatobiliary cancer after hepatocellular carcinoma. Cholangiocarcinoma is an uncommon tumor; between 2500

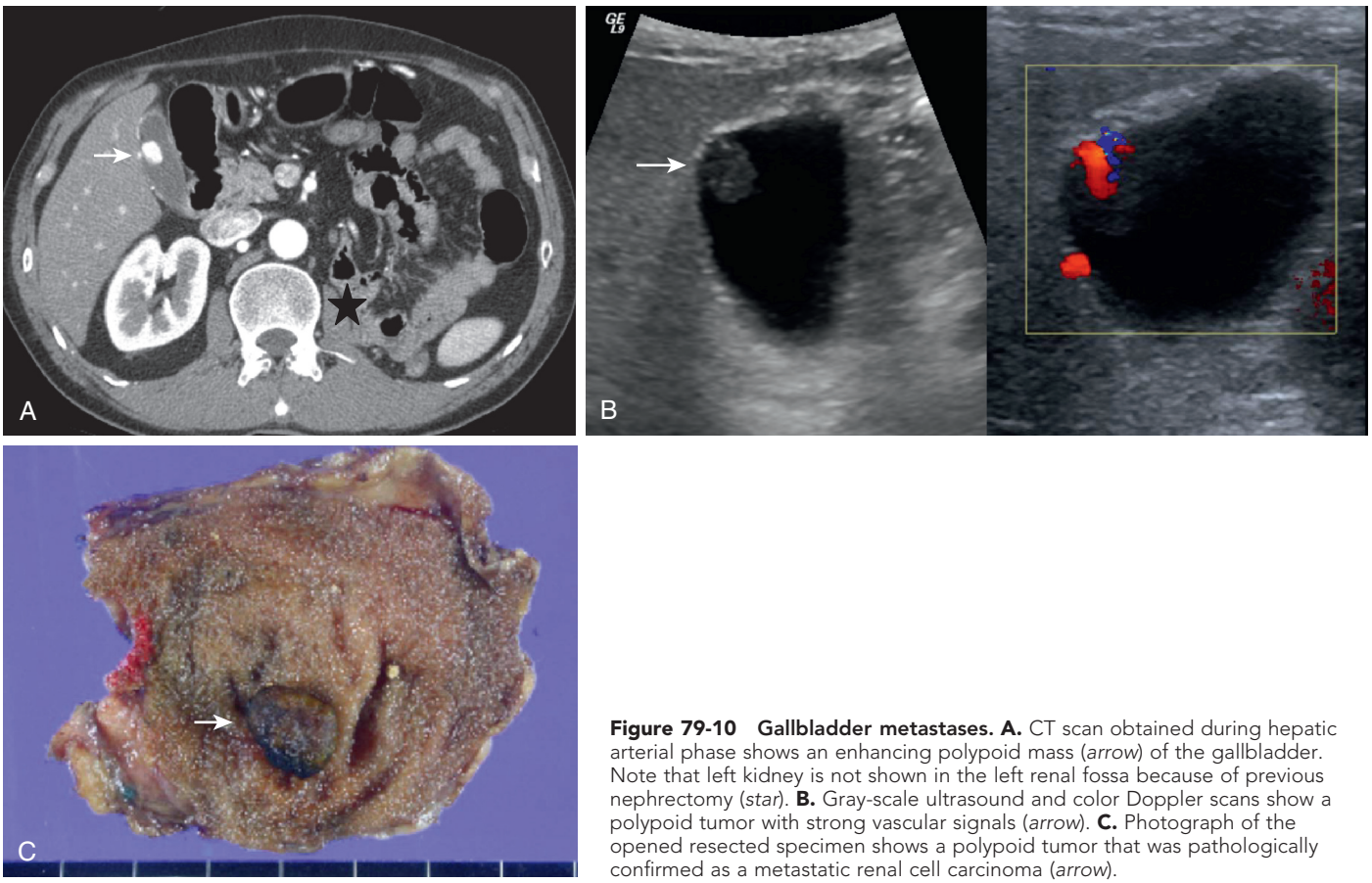

Figure 79-10 Gallbladder metastases. A. CT scan obtained during hepatic arterial phase shows an enhancing polypoid mass (*arrow*) of the gallbladder. Note that left kidney is not shown in the left renal fossa because of previous nephrectomy (*star*). **B.** Gray-scale ultrasound and color Doppler scans show a polypoid tumor with strong vascular signals (*arrow*). **C.** Photograph of the opened resected specimen shows a polypoid tumor that was pathologically confirmed as a metastatic renal cell carcinoma (*arrow*).

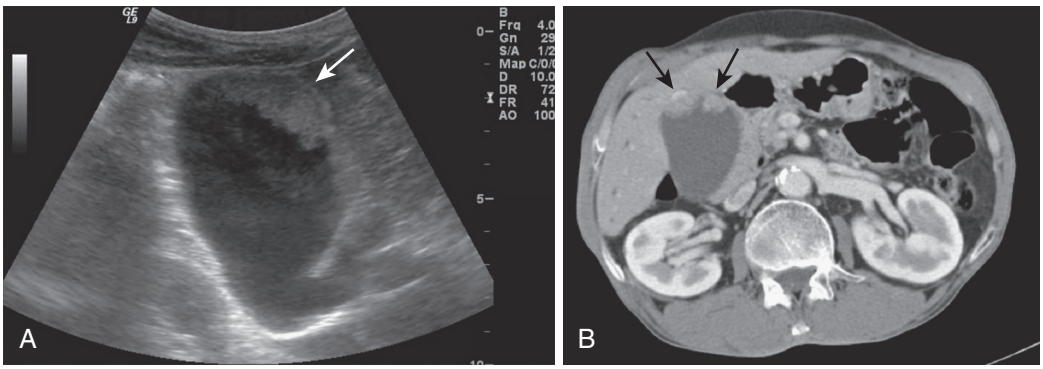

Figure 79-11 Gallbladder adenoma. A. Sonogram shows a sessile polypoid mass (*arrow*). **B.** CT scan demonstrates an enhancing polypoid gallbladder adenoma (*arrows*).

and 3000 new cases of cholangiocarcinoma are diagnosed annually in the United States.[4,18,19] This tumor is more prevalent in the Far East and Southeast Asia, where liver fluke infection and choledocholithiasis are common. Cholangiocarcinomas occur slightly more often in men, with a male-to-female ratio of 1.3:1; the average age at diagnosis is between 50 and 70 years.[67] Risk factors for this neoplasm include primary sclerosing cholangitis, choledochal cyst, familial polyposis, congenital hepatic fibrosis, bile duct stone disease, prior biliary-enteric anastomosis, infection with the Chinese liver fluke *Clonorchis sinensis*, and history of exposure to thorium dioxide (Thorotrast).[68,69]

PATHOLOGIC FINDINGS

More than 95% of cholangiocarcinomas are adenocarcinomas originating from bile duct epithelium. Most cholangiocarcinomas are well to moderately differentiated adenocarcinomas with a tendency to develop desmoplastic reactions and early perineural invasion.[69] Cholangiocarcinoma is classified anatomically into three groups: intrahepatic and peripheral to the liver hilum, hilar, or extrahepatic. These three types of cholangiocarcinoma are regarded as distinct disease entities therapeutically. Intrahepatic tumors are treated with hepatectomy, when possible, and hilar tumors are managed with resection of the bile duct, preferably with hepatectomy. Extrahepatic tumors are treated in a fashion similar to other periampullary malignant neoplasms with pancreatoduodenectomy. Although their precise definitions are controversial, a tumor that arises peripheral to the secondary bifurcation of the left or right hepatic duct is considered an intrahepatic cholangiocarcinoma. A tumor that arises from one of the hepatic ducts or from the bifurcation of the common hepatic duct is classified as a hilar cholangiocarcinoma.[70] Peripheral intrahepatic cholangiocarcinoma accounts for 10% of all cholangiocarcinomas, hilar cholangiocarcinoma for 25%, and extrahepatic cholangiocarcinoma for 65%.[71]

Cholangiocarcinomas are also divided into three types on the basis of their morphology: mass forming; periductal infiltrating, causing stricture; and intraductal growing.[71-75] This morphologic classification of cholangiocarcinoma is of great importance as it reflects biologic behavior and mode of spread of the tumor, and different types of cholangiocarcinoma may need different staging systems or different treatment strategies[73,74] Mass-forming intrahepatic cholangiocarcinoma is a gray-white mass often accompanied by satellite nodules (Fig. 79-12). Fibrosis and necrosis are frequently seen centrally. The periductal infiltrating type of cholangiocarcinoma grows along the bile duct wall, resulting in concentric mural thickening and proximal dilation.[73] A dense fibroblastic reaction may encase the adjacent hepatic artery or portal vein, complicating surgical resection (Fig. 79-13).[75-77] Intraductal growing papillary cholangiocarcinoma is characterized by the presence of intraluminal papillary tumors of the intrahepatic or extrahepatic bile ducts with partial obstruction and dilation of the bile ducts (Fig. 79-14).[72] The tumors are usually small but often spread superficially along the mucosal surface, resulting in multiple tumors along the adjacent segments of the bile ducts or a tumor cast.[78] Some papillary tumors of the bile ducts produce a large amount of mucin and may impede the flow of bile.[74,75,78] Ducts both proximal and distal to the tumor can be dilated because mucin may obstruct the papilla of Vater.

CLINICAL FINDINGS

Patients with hilar or extrahepatic cholangiocarcinomas usually present with painless jaundice. Anorexia, weight loss, vague gastrointestinal symptoms, ill-defined upper abdominal discomfort, and elevated serum alkaline phosphatase and bilirubin levels also can be seen. Cholangitis is unusual as a presenting symptom but most commonly develops after biliary manipulation. Patients with intrahepatic cholangiocarcinoma are usually asymptomatic and are rarely jaundiced until late in the course of disease.

RADIOGRAPHIC FINDINGS

The radiologic evaluation of patients with cholangiocarcinoma should delineate the overall extent of the tumor, including involvement of the bile ducts, liver, and portal vessels and distant metastases.[19] Various imaging tests are available to assess patients with cholangiocarcinoma, and the initial radiographic studies consist of either ultrasound or CT. Ultrasound can quickly establish the level of biliary obstruction. Nowadays, MDCT has become the noninvasive diagnostic test of choice for detailed evaluation and staging of cholangiocarcinoma[76,77] as it is widely available and able to indicate the location of the tumor and show the relationship between adjacent tissues, such as hepatic artery, portal vein, and liver parenchyma. In addition, it also helps survey the entire abdomen for disease staging. In most centers, ERCP or percutaneous transhepatic cholangiography is used to evaluate the extent of biliary involvement and to provide palliation for jaundice.[76-78] MRI with MRCP offers the potential of evaluating parenchymal, vascular, biliary, and

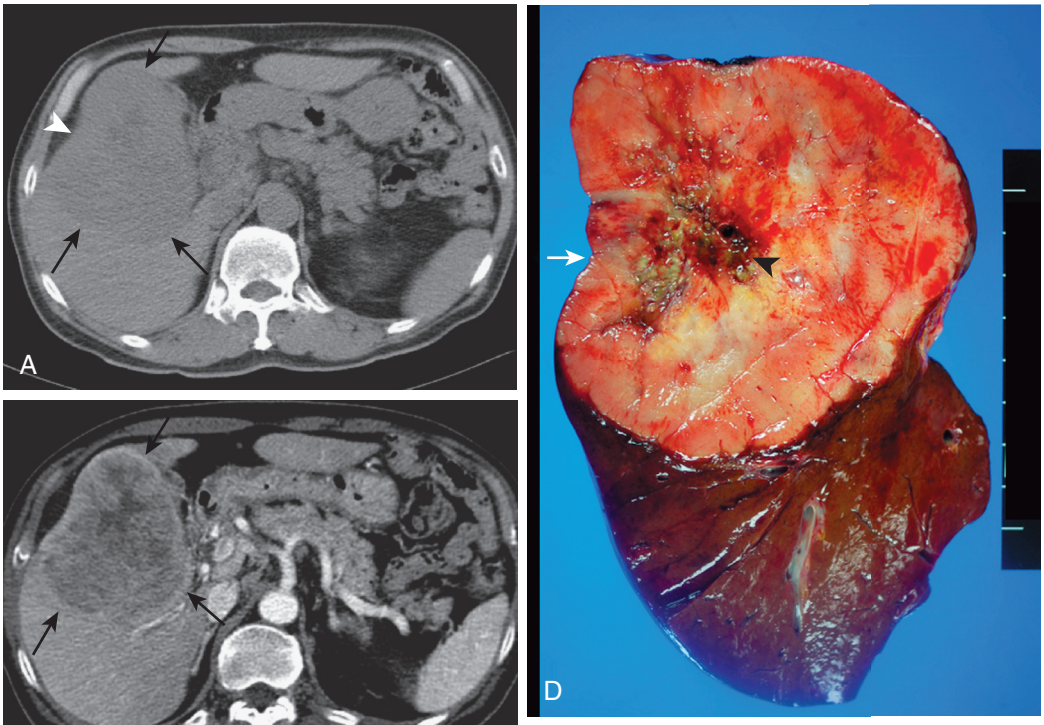

Figure 79-12 Intrahepatic mass-forming type of cholangiocarcinoma. A. Unenhanced CT shows a low-density mass (*arrows*) with focal capsular retraction (*arrowhead*). **B.** Hepatic arterial phase CT shows a nonspecific, malignant-appearing mass with peripheral enhancement (*arrows*) in the right lobe of the liver. **C.** Portal venous phase scan shows a gradual enhancement of the tumor (*arrows*) except for central nonenhancing necrotic foci. **D.** Photograph of the resected specimen shows a gray-white mass with capsular retraction (*arrow*). Fibrosis and central necrosis (*arrowhead*) are seen in the center.

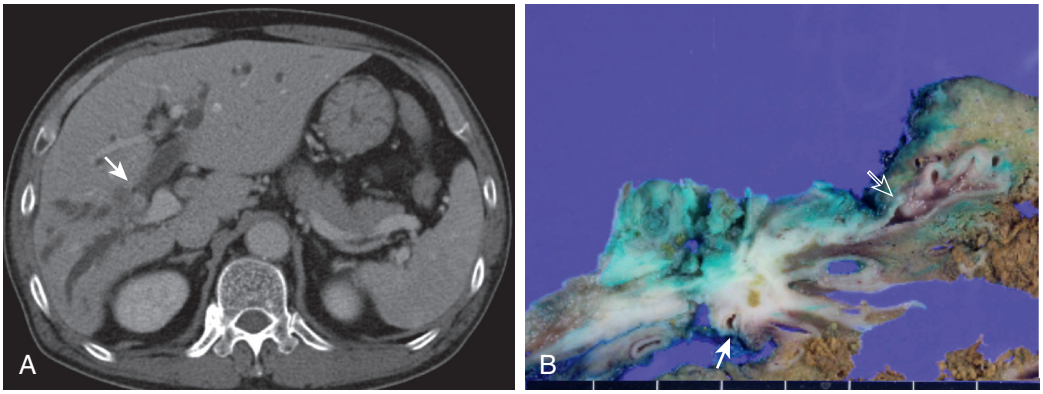

Figure 79-13 Periductal infiltrating type of cholangiocarcinoma. A. Portal venous phase scan shows a luminal narrowing of right intrahepatic bile duct with wall thickening (*arrow*) with invasion into adjacent hepatic parenchyma and upstream ductal dilation. Note dilation of left intrahepatic bile duct, suggestive of liver fluke (*Clonorchis sinensis*) infestation. **B.** Photograph of the resected specimen of a periductal infiltrating cholangiocarcinoma shows irregular thickening of the right main hepatic duct, with parenchymal invasion (*arrow*) as well as upstream ductal dilation (*open arrow*).

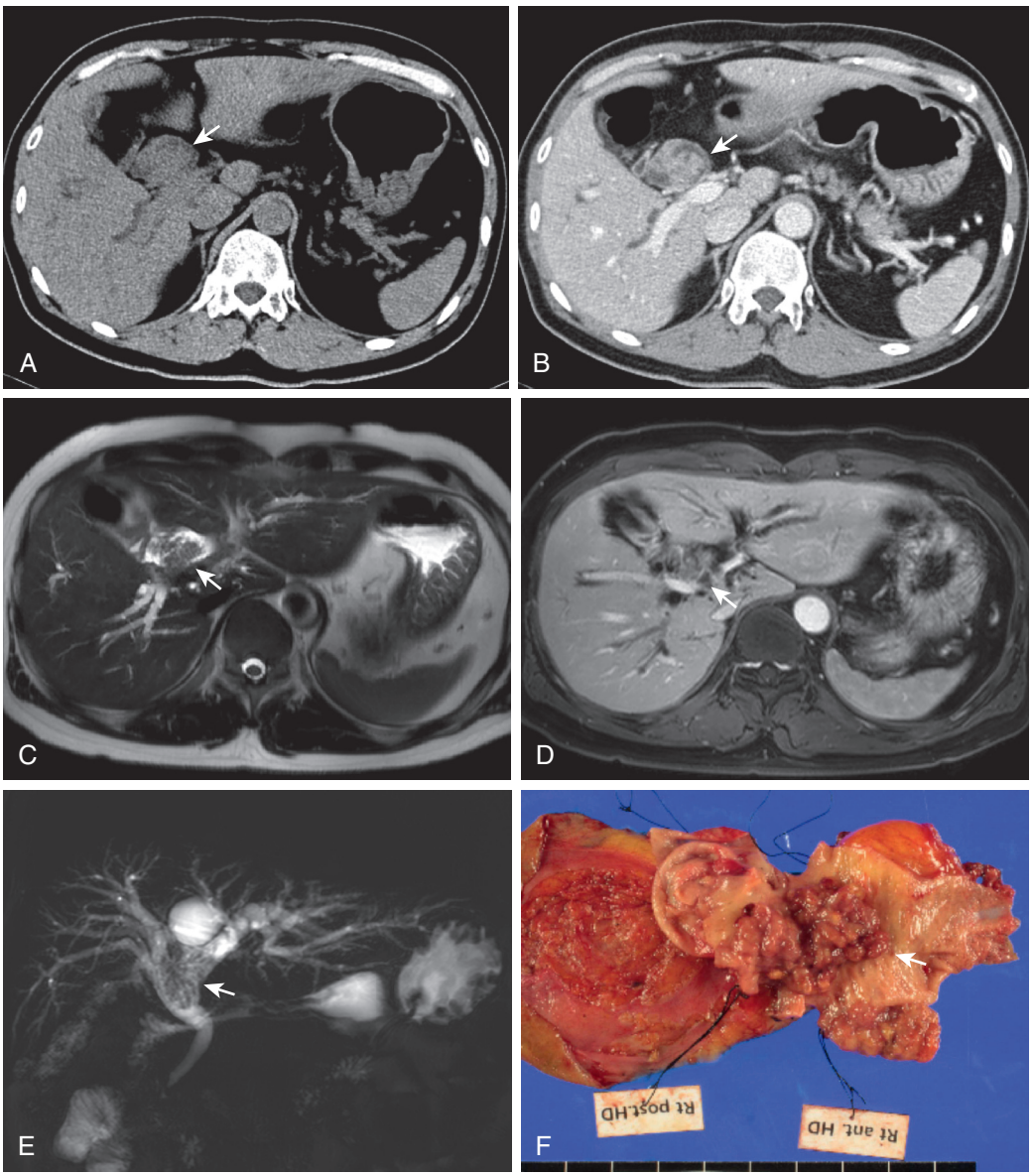

Figure 79-14 Intraductal growing papillary cholangiocarcinoma. A and **B.** Precontrast and postcontrast CT scans show an intraluminal tumor with papillary projections with weak enhancement (*arrow*) in the dilated hilar duct. **C.** Axial T2-weighted image shows a papillary cholangiocarcinoma (*arrow*) in the hilar duct. **D.** Contrast-enhanced axial T1-weighted image demonstrates a heterogeneously enhancing polypoid tumor (*arrow*) in the dilated common bile duct. **E.** MR cholangiography shows a papillary intraductal mass (*arrow*) at the hilar portion of the common bile duct with dilation of bilateral intrahepatic duct. **F.** Photograph of the resected specimen shows a large papillary tumor in left hepatic duct and common bile duct (*arrow*).

nodal involvement with a single noninvasive examination[77] (see Chapter 80). Although both MDCT and MRI with MRCP showed excellent diagnostic capability for assessing the longitudinal extent and tumor resectability of bile duct cancer, in general, MDCT or MRI generally underestimates the tumor involvement of vessels and lymph nodes.[79,80] The imaging features of cholangiocarcinoma depend on tumor location and type.

Intrahepatic Type

The most common appearance of a mass-forming cholangiocarcinoma on sonography, CT, and MRI is a well-defined, predominantly homogeneous mass with irregular borders.[81,82] On sonographic examination, these masses may have mixed echogenicity or may be predominantly hypoechoic or hyperechoic. Because of the peripheral location of the mass, bile duct obstruction is uncommon. Unenhanced CT scans show a hypoattenuating mass, either solitary or with satellite lesions (see Fig. 79-12). After the administration of contrast medium, there is irregular peripheral and patchy enhancement in the tumor. The dense fibrotic nature of the tumor often produces capsular retraction. Small necrotic regions and focal intrahepatic bile duct dilation around the mass are common.[82] A higher incidence of cholangiocarcinoma is associated with clonorchiasis (Fig. 79-15). The CT appearance of clonorchiasis is diffuse, mild dilation of the intrahepatic biliary ducts, especially the peripheral portions, without any evidence of obstruction.[83] Capsular retraction, dilation of the peripheral bile ducts, and presence of satellite nodules are frequent findings accompanying mass-forming intrahepatic cholangiocarcinoma.[82-85]

The typical appearance of cholangiocarcinoma on MRI is a nonencapsulated mass that is hypointense on T1-weighted images and hyperintense on T2-weighted images[84] (Fig. 79-16). Central hypointensity corresponding to fibrosis may be seen on T2-weighted images. Capsular retraction is found in 21% of mass-forming cholangiocarcinomas and seems to be related to the dense fibrotic nature of the tumor.[84,86] In addition, in patients with associated clonorchiasis, dilation of the peripheral

portion of the intrahepatic bile ducts is occasionally seen. Cholangiography demonstrates displacement of bile ducts away from the intrahepatic cholangiocarcinoma, obstruction of an intrahepatic duct, or a polypoid mass in the intrahepatic ducts.

Exophytic, intrahepatic cholangiocarcinomas simulate other hepatic malignant neoplasms, particularly hepatocellular carcinoma, on cross-sectional imaging. Most cholangiocarcinomas, however, occur in noncirrhotic livers. In addition, on dynamic CT or MRI, typical mass-forming cholangiocarcinoma shows thin rimlike or thick bandlike enhancement around the tumor during the hepatic arterial and portal venous phases.[82,83,87] On delayed (10-15 minutes) scans, there is progressive and concentric filling of the contrast material[81,86] (see Fig. 79-16). The enhancement pattern of cholangiocarcinoma is explained by slow diffusion of contrast material into the interstitial spaces of the tumor.[84] This pattern differs from that of hepatocellular carcinoma, which typically shows robust enhancement in the hepatic arterial phase and isoattenuation or low attenuation on the portal venous phase.[85] A study[86] reported that hepatobiliary phase imaging of gadoxetic acid–enhanced MRI could improve detection of daughter nodules and intrahepatic metastases compared with dynamic phase images, which might be beneficial for staging and surgical planning of mass-forming cholangiocarcinomas. Hypovascular metastases, especially from adenocarcinoma of the gastrointestinal tract, may show an enhancement pattern similar to that of peripheral cholangiocarcinomas. Absence of a known primary malignant neoplasm, relatively large tumor size, and bile duct dilation favor mass-forming cholangiocarcinomas over metastases.[81]

Intrahepatic cholangiocarcinomas may also be polypoid or focally stenotic (Fig. 79-17). If exophytic intrahepatic cholangiocarcinomas are excluded, about three fourths of cholangiocarcinomas are manifested as a focal stricture, and one fourth are polypoid or diffusely stenotic.[87] Focally stenotic or papillary cholangiocarcinomas often cause segmental bile duct dilation and may induce lobar atrophy if the tumor is central in location. Papillary intrahepatic cholangiocarcinoma occasionally produces abundant mucin, resulting in a well-marginated cystic

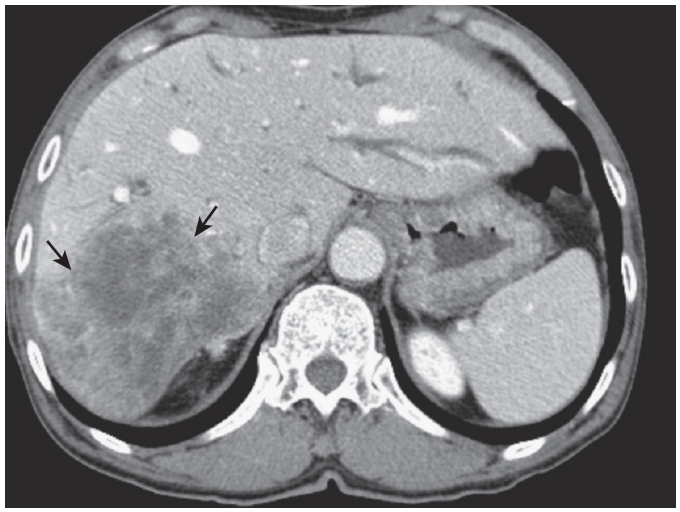

Figure 79-15 Intrahepatic cholangiocarcinoma associated with clonorchiasis. Contrast-enhanced CT scan shows an irregular low-density cholangiocarcinoma (*arrows*) in the right lobe of the liver and mild, diffuse dilation of intrahepatic bile ducts, suggesting clonorchiasis.

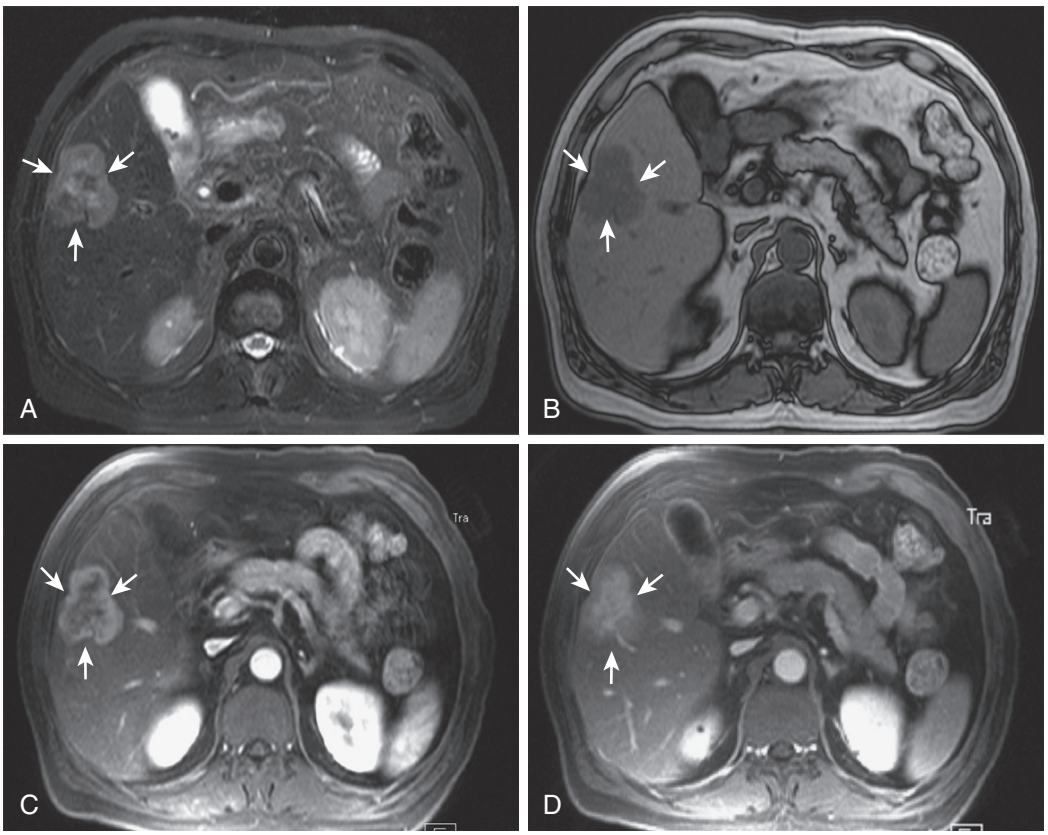

Figure 79-16 Intrahepatic cholangiocarcinoma. **A.** T2-weighted turbo spin-echo image shows a heterogeneously hyperintense cholangiocarcinoma (*arrows*) in the right lobe of the liver. **B.** Opposed-phase T1-weighted MR image demonstrates a hypointense mass (*arrows*). **C** and **D.** Dynamic gadolinium-enhanced T1-weighted gradient-echo images at 1 and 5 minutes after injection of contrast material reveal progressive centripetal enhancement of the tumor (*arrows*).

mass that resembles biliary cystadenocarcinoma (Fig. 79-18). A correct diagnosis of intraductal cholangiocarcinoma can be made by demonstrating direct continuity of the peripheral bile ducts with the tumor and incorporated hepatic parenchyma between cysts.[88,89] Mucin may result in tumor calcification and can also obstruct the duct lumen distal to the carcinoma (Fig. 79-19).

Hilar Type

Cholangiocarcinomas most often occur at the confluence of the right and left bile ducts and the proximal common hepatic duct.

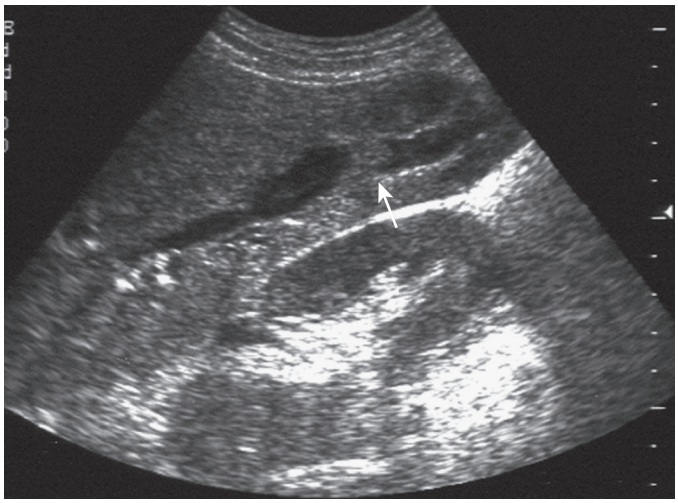

Figure 79-17 Papillary cholangiocarcinoma. Sonogram shows a papillary cholangiocarcinoma filling the dilated right intrahepatic bile duct (*arrow*).

These so-called Klatskin's tumors are usually periductal infiltrating types.[90-92] The sonographic features of Klatskin's tumors include duct dilation, isolation of the right and left bile duct segments, mass or bile duct wall thickening at the hilum, and lobar atrophy with crowded, dilated bile ducts.[92,93] Klatskin's tumors almost invariably cause biliary dilation. Although the tumor can appear as mural thickening or an encircling mass along the bile duct wall, a definite mass is rarely seen on ultrasound[90-94] (Fig. 79-20). Less often, a polypoid mass can cause hilar obstruction.

CT is more sensitive than ultrasound in detecting obstructing ductal masses, which are usually small (Fig. 79-21). MDCT allows more accurate evaluation of these small lesions and better demonstrates the status of the hepatic arterial or portal venous circulation.[92] The mass is hypodense to liver on most scans before administration of contrast material.[81] On contrast-enhanced CT, infiltrating tumors are seen as a focal thickening of the duct wall, obliterating the lumen. About 80% of these tumors are hyperattenuating relative to the liver on arterial or portal phase or both (see Fig. 79-13).[91,92,95] Because of their sclerotic nature, most lesions show delayed tumor enhancement up to 8 to 15 minutes after injection of contrast medium (Fig. 79-22).[95,96]

Cholangiocarcinomas are either isointense or low in signal intensity relative to the liver on T1-weighted images. On T2-weighted images, the tumor signal intensity ranges from markedly increased to mildly increased relative to liver. Tumors with high fibrous content tend to have lower signal intensity on T2-weighted images[98] (Fig. 79-23). Cholangiocarcinomas enhance to a moderate degree on gadolinium-enhanced T1-weighted MR images. MRI with MR cholangiography can provide comprehensive evaluation of axial and longitudinal tumor extent of hilar cholangiocarcinomas as well as of vascular

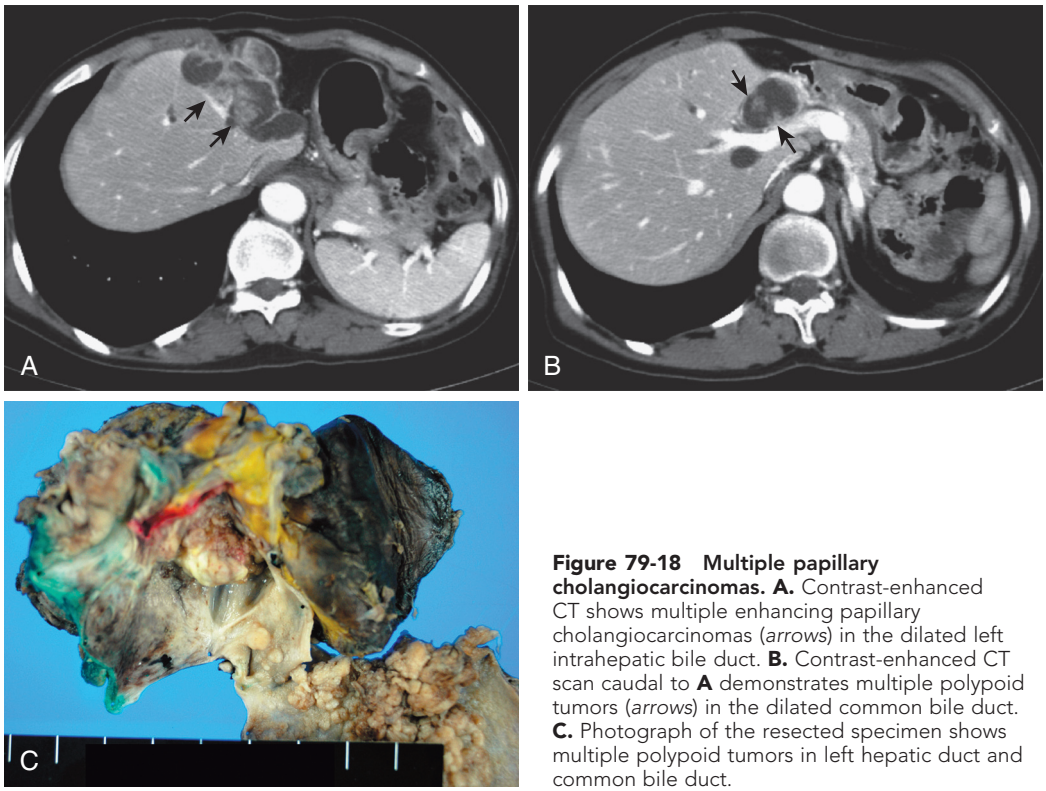

Figure 79-18 Multiple papillary cholangiocarcinomas. A. Contrast-enhanced CT shows multiple enhancing papillary cholangiocarcinomas (*arrows*) in the dilated left intrahepatic bile duct. **B.** Contrast-enhanced CT scan caudal to **A** demonstrates multiple polypoid tumors (*arrows*) in the dilated common bile duct. **C.** Photograph of the resected specimen shows multiple polypoid tumors in left hepatic duct and common bile duct.

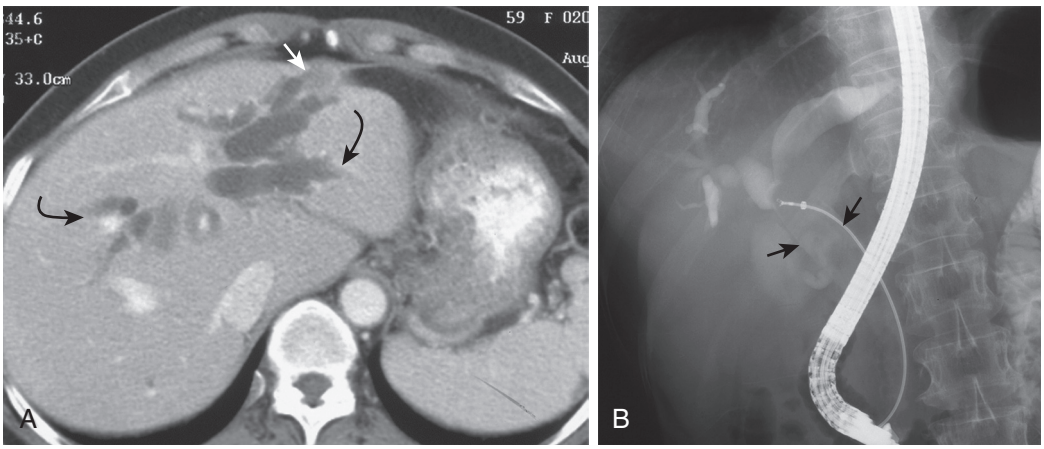

Figure 79-19 Mucin-secreting cholangiocarcinoma. A. CT shows a polypoid mass (*arrow*) in the left hepatic lobe and dilated left and right intrahepatic bile ducts (*curved arrows*) and dilated left and common hepatic bile ducts. **B.** ERCP demonstrates mucin expanding the extrahepatic bile ducts (*arrows*). At endoscopy, mucin was seen coming from the common bile duct.

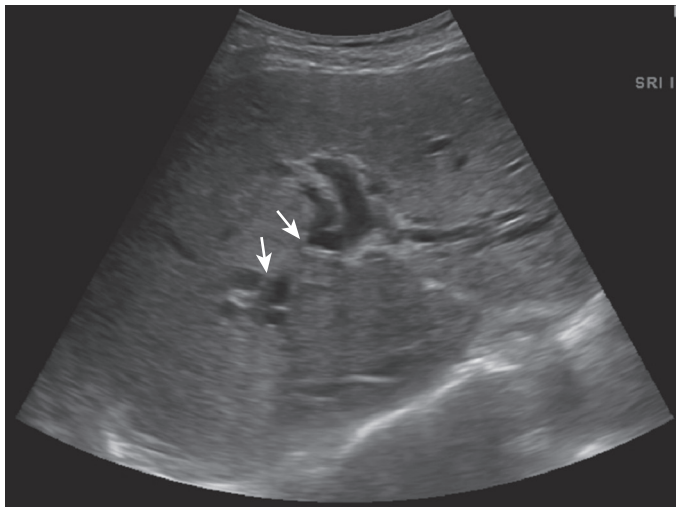

Figure 79-20 Klatskin's tumor. Sonography of Klatskin's tumor shows dilation of intrahepatic bile ducts and nonunion of right and left intrahepatic bile ducts (*arrows*).

involvement by the tumors[77,99,100] (Fig. 79-24). As with CT, contrast enhancement is better appreciated on delayed images because of the nature of the tumor (Fig. 79-25).

Lobar hepatic atrophy with marked dilation and crowding of bile ducts is seen on CT and MRI in approximately one fourth of patients with hilar cholangiocarcinomas.[94] There is dominant involvement of the duct supplying the atrophied segment. Lobar hepatic atrophy with biliary dilation strongly suggests cholangiocarcinoma, although long-standing biliary obstruction from surgical trauma or focal biliary obstruction can cause similar findings (see Fig. 79-24).[58,92,100] The liver parenchyma and hepatoduodenal ligaments are commonly invaded by Klatskin's tumors.[70,90,92,101] Lymphatic metastases most commonly involve the portocaval, superior pancreaticoduodenal, and posterior pancreaticoduodenal lymph nodes.[54] Retroperitoneal lymphadenopathy, peritoneal spread, and proximal intestinal obstruction occur in advanced stages of hilar cholangiocarcinoma.

Although periductal infiltrating cholangiocarcinoma is the most common type of hilar cholangiocarcinoma, less often, intraductal growing cholangiocarcinoma can occur in the hilar duct. The intraductal tumors may show higher attenuation than bile on precontrast CT images and hypoenhancement with regard to the hepatic parenchyma on contrast-enhanced images, probably because of lack of fibrotic stroma[97] (see Fig. 79-14). When intraductal tumors are developed as multiple intraluminal lesions, they can be easily mistaken for intrahepatic duct stones or extrahepatic bile duct stones.[98,99] Contrast enhancement of the intraluminal lesions on contrast-enhanced CT or MRI can differentiate intraductal growing type cholangiocarcinoma from stones (see Fig. 79-14).[97,98]

In patients with hilar cholangiocarcinoma, accurate evaluation of tumor extent is necessary for proper treatment and assessment of resectability.[19] Nonresectability of hilar cholangiocarcinoma is suggested by cholangiographic evidence of severe bilateral involvement of the secondary confluence (see Fig. 79-24), involvement of the main trunk of the portal vein, involvement of both branches of the portal vein or bilateral involvement of the hepatic artery and portal vein, or vascular involvement on one side of the liver and extensive bile duct involvement on the other side.[100-102] Unilateral involvement of the hepatic artery or portal vein or both vessels is compatible with resection.[18,19,100] Precise preoperative evaluation of tumor extent often requires several imaging studies.[77]

Direct cholangiography (Fig. 79-26) is used to evaluate the extent of hilar cholangiocarcinomas.[77,79] There is characteristic stenosis of the central, right, and left common hepatic ducts, with smooth shoulders or irregular tapering of ducts. These neoplastic strictures tend to branch and may extend into second-order biliary radicles. Direct cholangiography is of limited value in assessing submucosal tumor spread and lesions that extend beyond the porta hepatis because of incomplete filling of bile ducts proximal to the tumor. In addition, CT is ineffective in detecting superficially spreading tumors that extend above the level of biliary obstruction because tumor with a superficial spreading pattern shows enhancement of the inner wall of the bile duct with a preserved lumen.[70] Therefore, combined assessment with CT and state-of-the-art cholangiography or choledochoscopy (through the percutaneous transhepatic biliary drainage tract) and biopsy are needed to evaluate tumor extent.[70,81] Along these lines, a combination of MRCP and conventional MRI can provide complete tumor staging

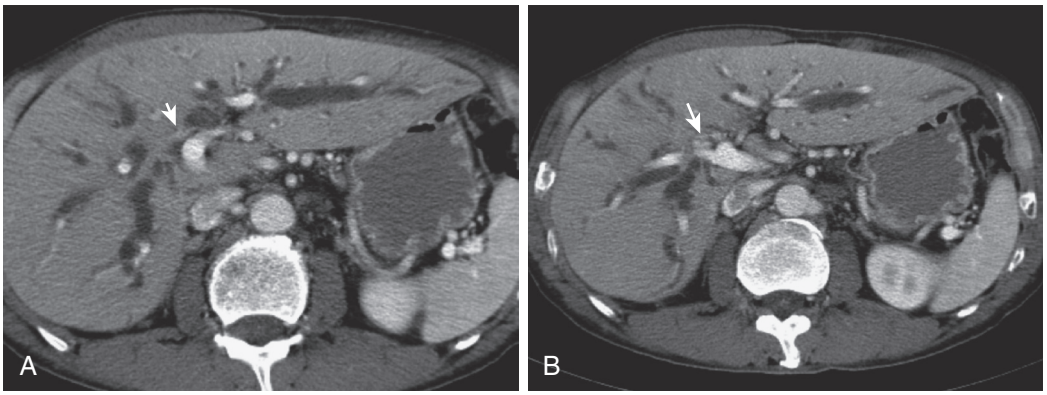

Figure 79-21 Contrast-enhanced CT scans reveal a small enhancing hilar cancers causing biliary strictures (*arrow*) involving central portion of the left (**A**) and right (**B**) bile duct.

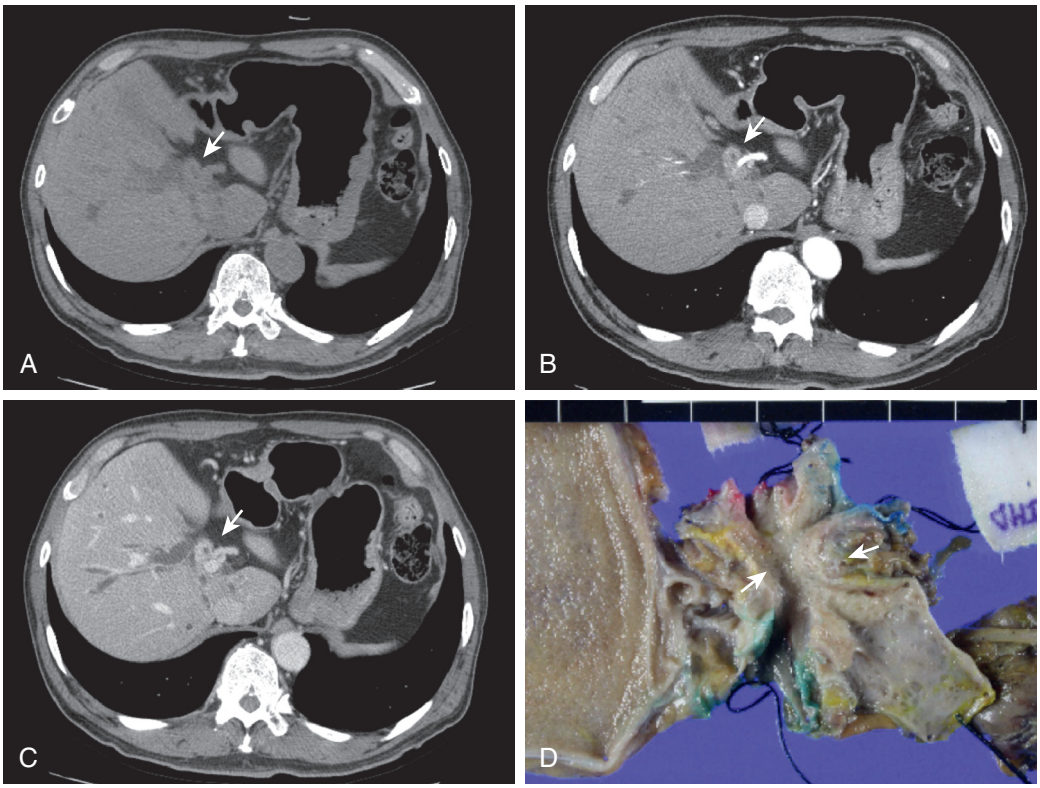

Figure 79-22 Hilar cholangiocarcinoma showing delayed hyperenhancement on CT. Contrast-enhanced CT scans during arterial phase (**A** and **B**) and delayed phase (**C**) reveal a homogeneously hyperenhancing, circumferential wall thickening of the hilar duct (*arrow*) with dilation of both the right and left bile ducts (not shown). Photograph of the resected specimen (**D**) shows a luminal narrowing and wall thickening (*arrows*) caused by an infiltrating cholangiocarcinoma involving the proximal common duct as well as bilateral main hepatic ducts.

that assesses liver, portal node, and portal vein involvement[79,102] (Fig. 79-27).

Hilar cholangiocarcinomas can usually be differentiated cholangiographically from hilar lymphadenopathy or benign stricture. However, differentiating between benign and malignant biliary strictures is sometimes challenging. Indeed, periductal infiltrating type cholangiocarcinomas, especially in the early stage, may be difficult to differentiate from benign strictures.[80,103,104] Lymphadenopathy compresses and displaces rather than invades the extrahepatic ducts. Benign strictures complicating cholecystectomy or distal gastric surgery are typically short and cause symmetric narrowing of the common hepatic bile duct.[103] Rarely, lymphoma or sarcoidosis of the bile ducts may be indistinguishable from cholangiocarcinoma.[102] Longer and thicker involvement, luminal irregularity, asymmetric narrowing, hyperenhancement during portal venous phase, periductal soft tissue lesion, and lymph node enlargement suggest a malignant stricture rather than a benign stricture[103-105] (see Figs. 79-25 and 79-26). Recently, great attention has focused on immunoglobulin G4 (IgG4)–related sclerosing cholangitis, which can often mimic periductal infiltrating cholangiocarcinoma. Imaging findings such as involvement of intrapancreatic common duct, smooth outer margin, symmetric narrowing of bile ducts, lower degree of dilation of upstream duct, and lower degree of contrast enhancement are more frequent in IgG4-related sclerosing cholangitis than in cholangiocarcinoma[106,107] (Fig. 79-28). In addition, coexisting autoimmune pancreatitis, good response to steroid therapy, and increase in IgG and IgG4 are helpful clinical and laboratory findings for the diagnosis of IgG4-related sclerosing cholangitis.[106,107]

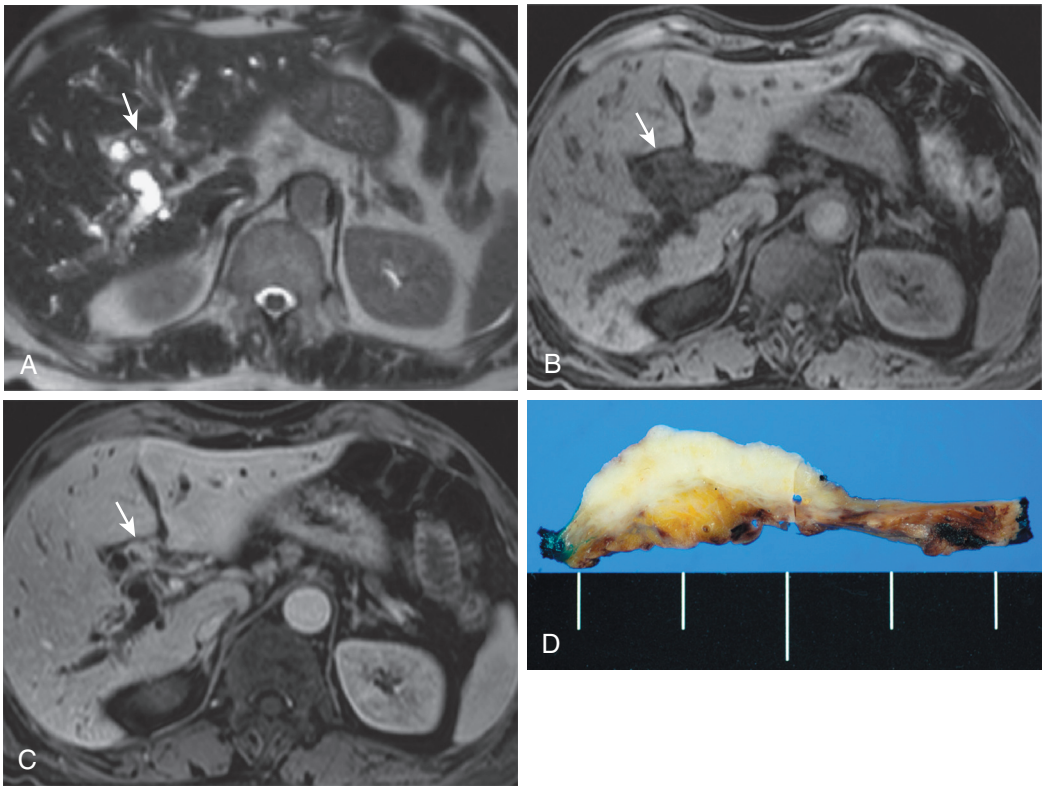

Figure 79-23 Hilar cholangiocarcinoma: MR findings. A. T2-weighed MR image shows a slightly hyperintense hilar cholangiocarcinoma (*arrow*). **B.** Fat-suppressed T1-weighted MR image reveals a hypointense hilar cholangiocarcinoma (*arrow*). **C.** Gadolinium-enhanced T1-weighted image demonstrates an enhancing mass (*arrow*) in left main hepatic duct. **D.** Photograph of the resected specimen shows an infiltrating cholangiocarcinoma involving the left main hepatic duct and proximal common duct.

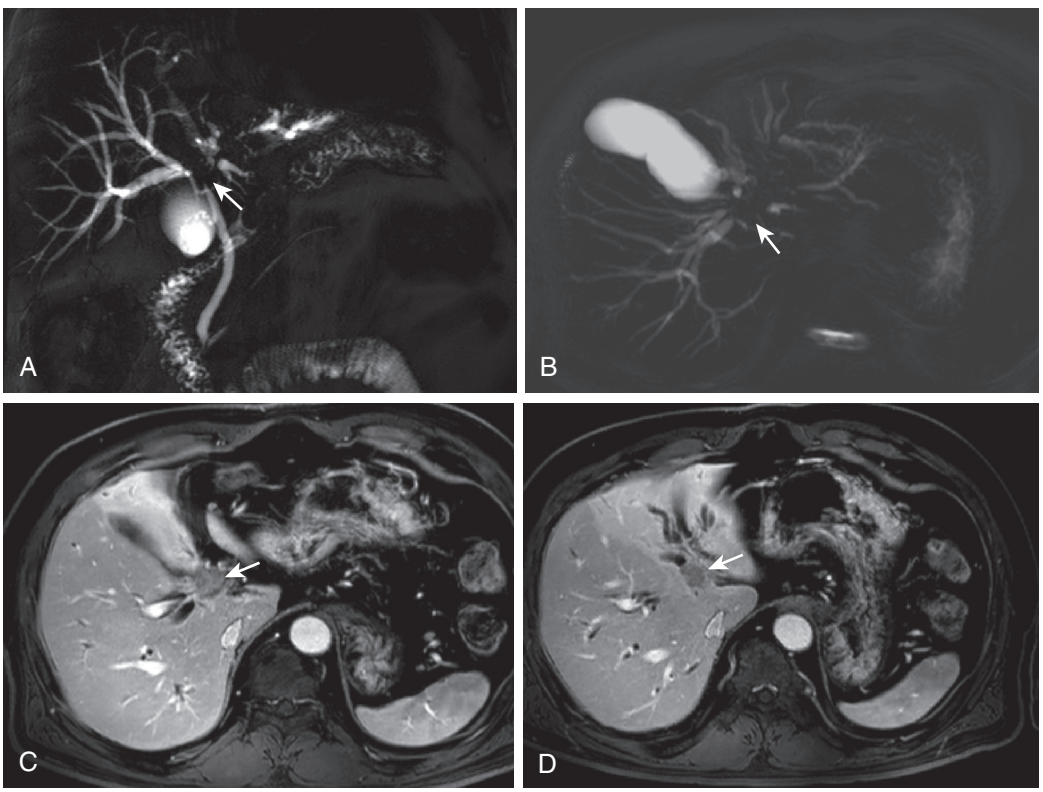

Figure 79-24 Comprehensive evaluation of hilar cholangiocarcinoma by MRI with MR cholangiography for surgical resectability. A and **B.** Coronal and axial thick-slab single-shot MR cholangiograms demonstrate hilar cholangiocarcinoma involving both secondary biliary confluences with upstream ductal dilation. Note that segmental intrahepatic ducts of the left lobe are separated by the tumor (*arrow*). **C** and **D.** Postcontrast T1-weighted MR images demonstrate a periductal infiltrating hilar cholangiocarcinoma involving ductal bifurcation area and both main hepatic ducts (*arrow*). The mass (*arrow*) shows hypoenhancement compared with adjacent liver parenchyma.

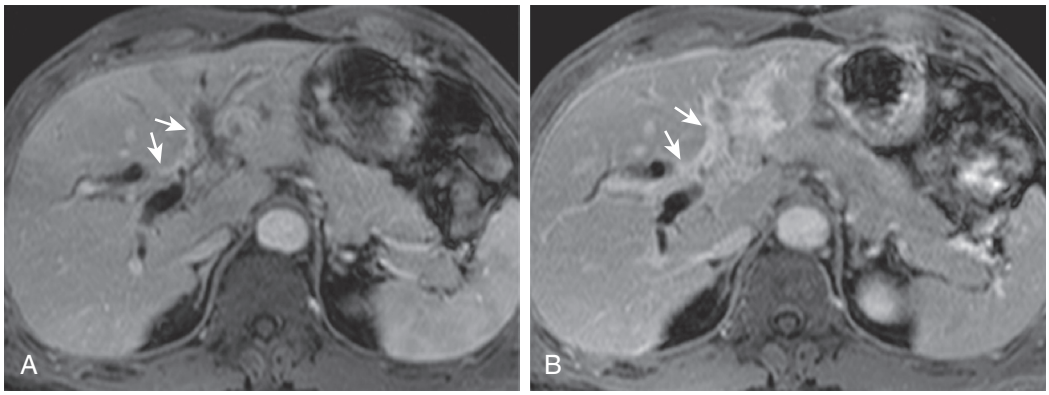

Figure 79-25 Delayed contrast enhancement of cholangiocarcinoma: MRI. A. Gadolinium-enhanced T1-weighted image obtained during portal venous phase shows an infiltrating hilar cholangiocarcinoma involving ductal bifurcation area and both main hepatic ducts (*arrows*). **B.** A 10-minute delayed T1-weighted MR image shows delayed enhancement of the mass (*arrows*). Tumor involves periportal fat with encased left portal vein.

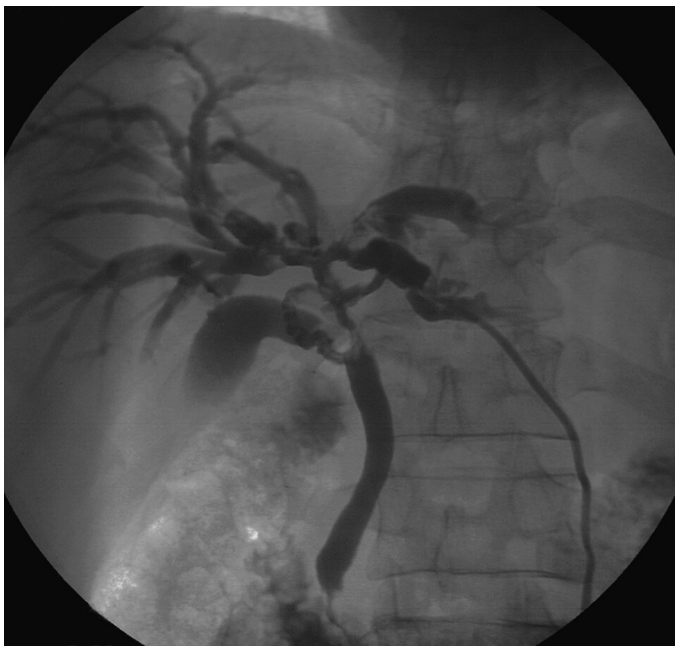

Figure 79-26 Cholangiogram of Klatskin's tumor. Hilar strictures are associated with proximal bile duct dilation.

Extrahepatic Type

Carcinomas of the distal common hepatic or common bile duct are usually small and have a better prognosis than the more central Klatskin's tumor.[18,19] Fifty percent to 75% of extrahepatic cholangiocarcinomas occur in the upper third, 10% to 30% in the middle third, and 10% to 20% in the lower third of the extrahepatic duct.[108] Cholangiography, either direct cholangiography or MR cholangiography, demonstrates a short stricture or, less often, a polypoid mass, which almost always causes biliary obstruction. CT and MRI can depict an obstructing nodular mass or a concentric or asymmetric thickening of the bile duct wall with enhancement at the transition zone or intraductal polypoid tumors as well as biliary ductal dilation[109] (Fig. 79-29). Adjacent periductal fat may be infiltrated by direct invasion, and lymph node metastasis is relatively frequent. Cholangiocarcinomas that arise in the intrapancreatic portion of the common bile duct are well depicted as low signal intensity masses against the background of the high signal intensity head of the pancreas on T1-weighted fat-suppressed images and as hyperenhanced thickening of the involved bile duct wall on contrast-enhanced T1-weighted images [110] (Fig. 79-30).

For patients with advanced primary sclerosing cholangitis, the risk for development of cholangiocarcinoma is significant. In one study, careful pathologic examination of the native liver removed for transplantation showed that 8% of patients with primary sclerosing cholangitis had coexisting cholangiocarcinoma.[111] It is often difficult to appreciate malignant degeneration in sclerosing cholangitis. Features that suggest malignancy include progression of strictures on serial cholangiograms, marked biliary dilation above a dominant stricture, and a polypoid ductal mass of 1 cm in diameter or greater[112] (Fig. 79-30).

Adults with fusiform extrahepatic choledochal cysts also are at increased risk for development of cholangiocarcinoma (Fig. 79-31). These neoplasms develop within the cyst itself in only about 50% of cases and elsewhere in the biliary system in the remainder. In fact, the cancer can occur after resection of the cyst.[113] Most are manifested as polypoid masses that may be large enough to be visible on cross-sectional imaging.

TREATMENT

Treatment of cholangiocarcinoma includes surgical resection, radiation, laser therapy, biliary stenting, systemic chemotherapy, and liver transplantation.[18,19,114] There are some long-term survivors after resection, and radiation and bile duct stenting may palliate symptoms for months to years.

Periampullary Carcinoma

Periampullary carcinomas are those tumors arising from or within 1 cm of the papilla of Vater and include ampullary, pancreatic, bile duct, and duodenal cancers.[115] It is often impossible by histologic examination to be certain of the origin of the tumor. There is a high incidence of these tumors in patients with familial adenomatous polyposis, and cancer is often preceded by ampullary or duodenal adenomas.[115] Periampullary neoplasms tend to be polypoid and lower in grade than more proximal biliary neoplasms.

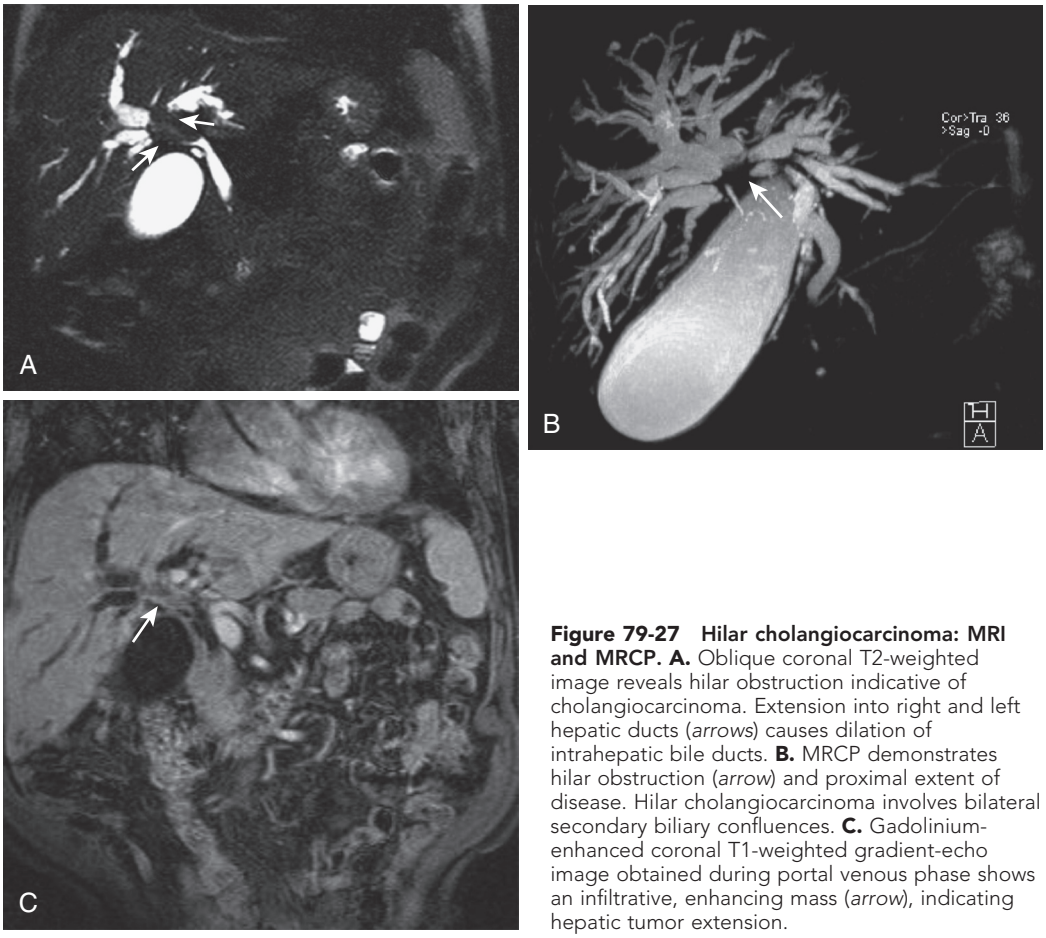

Figure 79-27 Hilar cholangiocarcinoma: MRI and MRCP. A. Oblique coronal T2-weighted image reveals hilar obstruction indicative of cholangiocarcinoma. Extension into right and left hepatic ducts (*arrows*) causes dilation of intrahepatic bile ducts. **B.** MRCP demonstrates hilar obstruction (*arrow*) and proximal extent of disease. Hilar cholangiocarcinoma involves bilateral secondary biliary confluences. **C.** Gadolinium-enhanced coronal T1-weighted gradient-echo image obtained during portal venous phase shows an infiltrative, enhancing mass (*arrow*), indicating hepatic tumor extension.

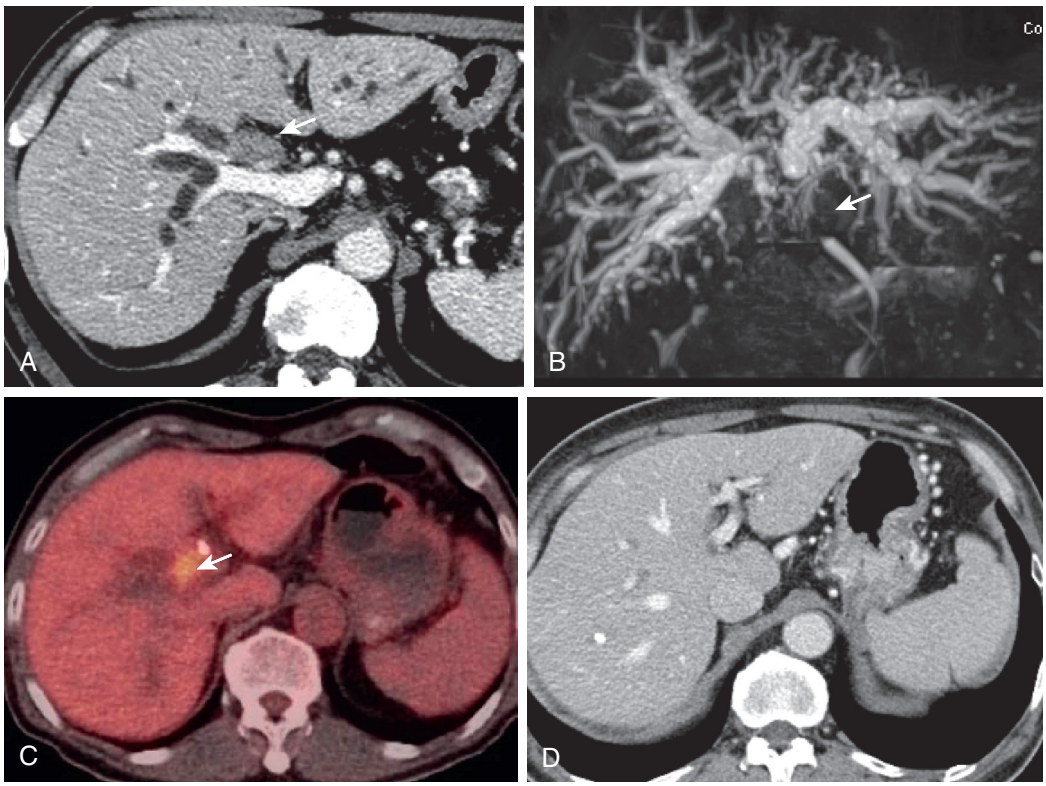

Figure 79-28 IgG4-related cholangitis mimicking cholangiocarcinoma. A. Axial CT during the portal venous phase shows a hypoenhancing mass (*arrow*) in common hepatic duct with upstream ductal dilation. **B.** Coronal MR cholangiography image demonstrates dilation of both intrahepatic ducts as well as a luminal narrowing (*arrow*) of common bile duct. **C.** ^{18}F-FDG PET/CT demonstrates a diffuse increased FDG activity of the hilar lesion (*arrow*). **D.** Follow-up CT scan after steroid treatment demonstrates complete resolution of the biliary stricture and upstream ductal dilation.

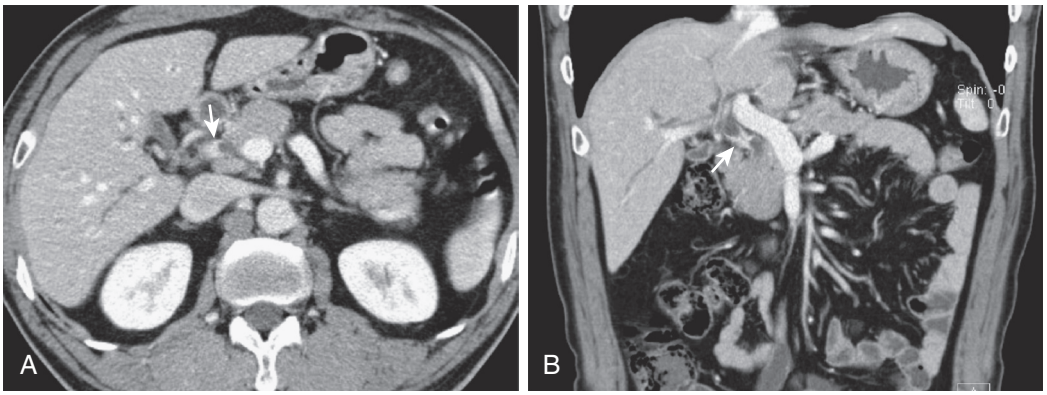

Figure 79-29 Extrahepatic cholangiocarcinoma. A. Axial CT during the portal venous phase shows an enhancing mass (*arrow*) in common bile duct. **B.** Coronal multiplanar reconstructed (MPR) image demonstrates focal mural thickening and enhancement (*arrow*) of common bile duct.

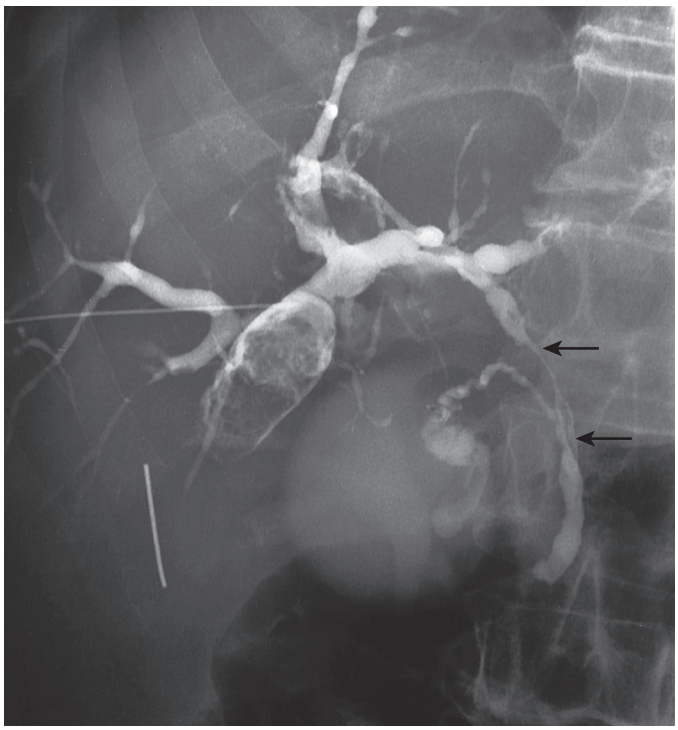

Figure 79-30 Cholangiocarcinoma complicating sclerosing cholangitis. Cholangiocarcinoma is causing a stricture (*arrows*) in the common hepatic duct in a patient with primary sclerosing cholangitis. Despite the dominant stricture with some biliary dilation proximally, this narrowing could be inflammatory or neoplastic. Calculi are present in the right intrahepatic bile ducts.

Biliary dilation to the level of the ampulla of Vater is seen in 75% of cases, and pancreatic ductal dilation is seen in 67%.[115] These masses tend to be small and may not be seen on CT scans, in which case abrupt termination of a dilated bile duct in the head of the pancreas is demonstrated, or abrupt termination of the common bile duct without mass may be seen on cholangiography.[116] Ampullary cancer can often be manifested as a polypoid mass at the ampulla with dilation of both main pancreatic duct and common bile duct on three-dimensional contrast-enhanced CT or MRI with MRCP[116] (Fig. 79-32). On occasion, a villous polypoid lesion may be seen in the distal common bile duct and duodenum. Liver metastasis or lymphadenopathy is present at the time of diagnosis in only a small percentage of cases.

On T1-weighted fat-suppressed images, periampullary tumors appear as a low signal intensity mass in the region of the ampulla. On immediate postgadolinium T1-weighted images, these lesions are often visualized as areas of low signal intensity, reflecting their hypovascular character compared with background pancreatic tissue.[116] On 2-minute postgadolinium fat-suppressed images, a thin rim of enhancement is commonly observed along the periphery of the tumor[58] (Fig. 79-33). MRCP and sectional MRI can be useful in determining the origins of periampullary carcinomas.

Cystic Bile Duct Neoplasms: Cystadenoma and Cystadenocarcinoma

Biliary cystadenoma and cystadenocarcinoma are rare cystic neoplasms lined by mucin-secreting columnar epithelium.[63] On histologic evaluation, they are similar to cystadenomas and cystadenocarcinomas of the ovary and pancreas. They are usually seen in middle-aged women, who present with abdominal pain, distention, and occasionally jaundice. Most cystadenomas and cystadenocarcinomas are manifested as intrahepatic masses that are hypoechoic on ultrasound and have a low-attenuation, uniloculated or multiloculated, cystic appearance on CT.[63] The CT attenuation of the fluid component in a biliary cystadenoma depends on the fluid content. Whereas CT is usually superior in demonstrating the size and extent of these tumors, sonography is superior to CT in depicting internal morphology[117] (Fig. 79-34). Irregular, papillary growths and mural nodules along the internal septa and wall are seen in cystadenoma and cystadenocarcinoma, although papillary excrescences and solid portions are more common in cystadenocarcinoma[117-119] (Fig. 79-35). Cystadenomas occasionally have fine septal calcifications; cystadenocarcinomas may have thick, coarse, mural, and septal calcifications.[117,118] Communication of these tumors with large intrahepatic ducts is rare. Several case reports have suggested malignant transformation of cystadenomas to cystadenocarcinomas on the basis of several years of follow-up after resection.[120,121] The differential diagnosis of biliary cystadenoma and cystadenocarcinoma includes hepatic cysts, hydatid cysts, liver abscesses, cystic metastases, hematoma, cystic sarcomas, and choledochal cysts.[117]

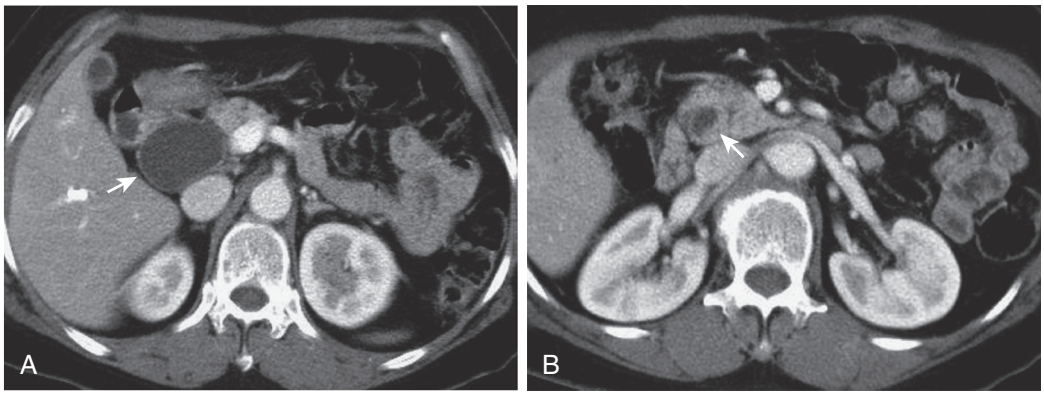

Figure 79-31 Cholangiocarcinoma complicating choledochal cyst. A. Contrast-enhanced axial CT scan shows a choledochal cyst (*arrow*). **B.** CT scan caudal to **A** shows an asymmetric thickening (*arrow*) of intrapancreatic common bile duct with enhancement.

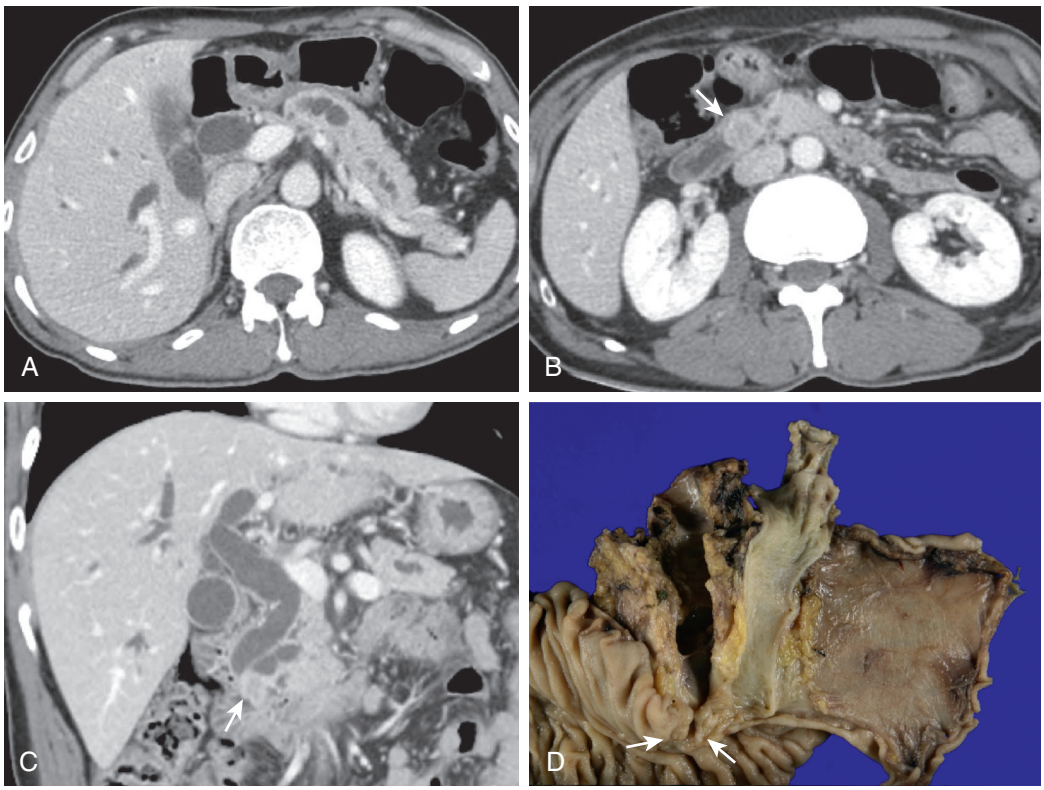

Figure 79-32 Ampulla of Vater cancer. A. Axial contrast-enhanced CT scan shows a dilation of the common bile duct and the main pancreatic duct. **B** and **C.** Axial and coronal contrast-enhanced CT scans show a hyperenhancing tumor (*arrow*) of the ampulla with extension into the main pancreatic duct. **D.** Photograph of the resected specimen shows an irregular mass of the ampulla of Vater (*arrows*) involving the distal common duct as well as the main pancreatic duct.

Other Malignant Neoplasms of the Bile Ducts

In adults, cholangiocarcinoma and biliary cystadenocarcinoma account for most malignant bile duct neoplasms. Lymphomas, leiomyosarcomas, carcinoid tumors, and metastases rarely occur in the bile ducts (Fig. 79-36). Non-Hodgkin's lymphoma of the bile ducts can rarely mimic cholangiocarcinoma or primary sclerosing cholangitis.[122,123] In a patient with known lymphoma, cholangiographic findings of smooth, tapered strictures combined with the absence of a portal mass on CT should suggest the diagnosis. Sarcomas and metastases are manifested as masses projecting into the bile duct lumen, causing biliary obstruction.[124,125]

After choledochal cyst, embryonal rhabdomyosarcoma is the second most common cause of jaundice in the pediatric population. After infancy, it usually occurs between the ages of 4 and 6 years but has been reported in children aged 1 to 11 years. Sonography and CT will show intrahepatic duct dilation and a soft tissue mass in the region of the common bile duct or porta hepatis. The radiologic appearance of the lesion is similar to that of congenital choledochal cyst if there is no local invasion to adjacent tissues.[126]

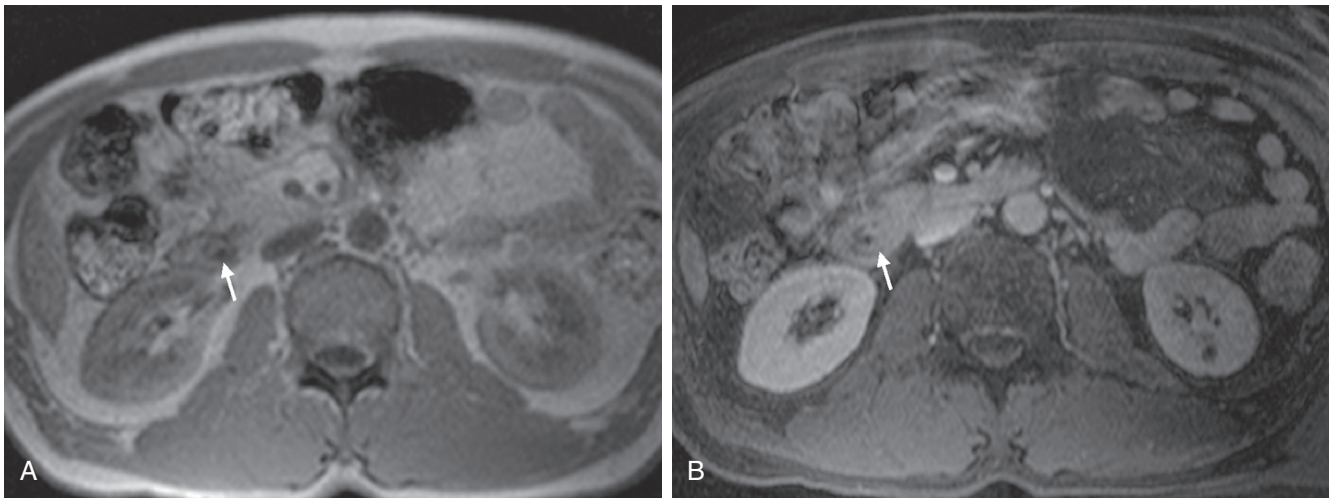

Figure 79-33 Ampullary cancer: MR findings. A. T1-weighted image shows a hypointense ampullary tumor (*arrow*). **B.** Postgadolinium fat-suppressed image demonstrates a thin rim of enhancement (*arrow*) along the periphery of the tumor.

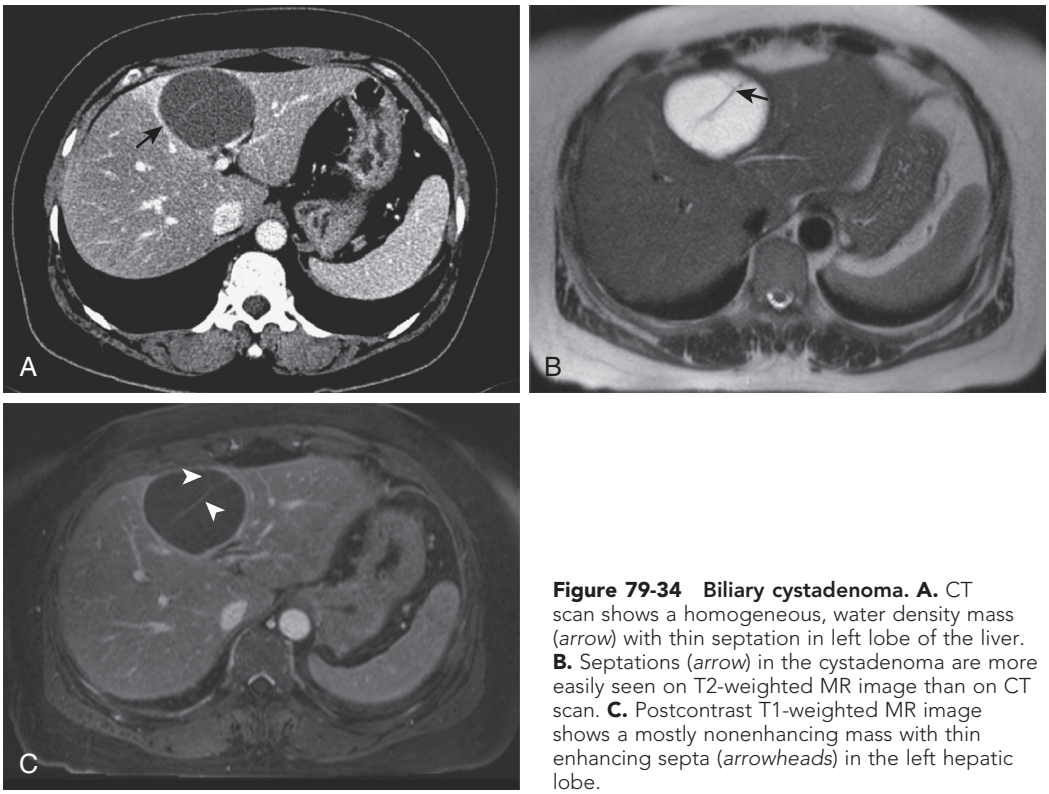

Figure 79-34 Biliary cystadenoma. A. CT scan shows a homogeneous, water density mass (*arrow*) with thin septation in left lobe of the liver. **B.** Septations (*arrow*) in the cystadenoma are more easily seen on T2-weighted MR image than on CT scan. **C.** Postcontrast T1-weighted MR image shows a mostly nonenhancing mass with thin enhancing septa (*arrowheads*) in the left hepatic lobe.

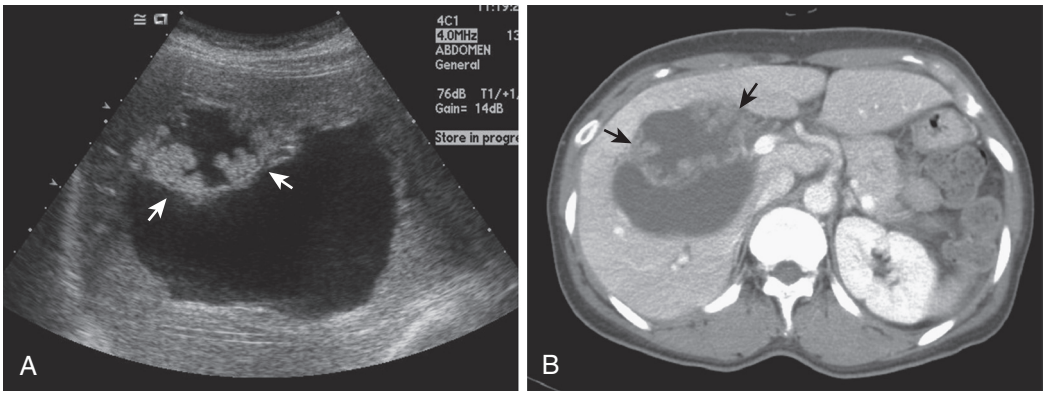

Figure 79-35 Biliary cystadenocarcinoma. A. Transverse sonogram shows a large, lobulated cystic mass with thick septation and multiple mural nodules (*arrows*). **B.** CT scan shows a lobulated cystic mass with thick septation and enhancing mural nodules (*arrows*).

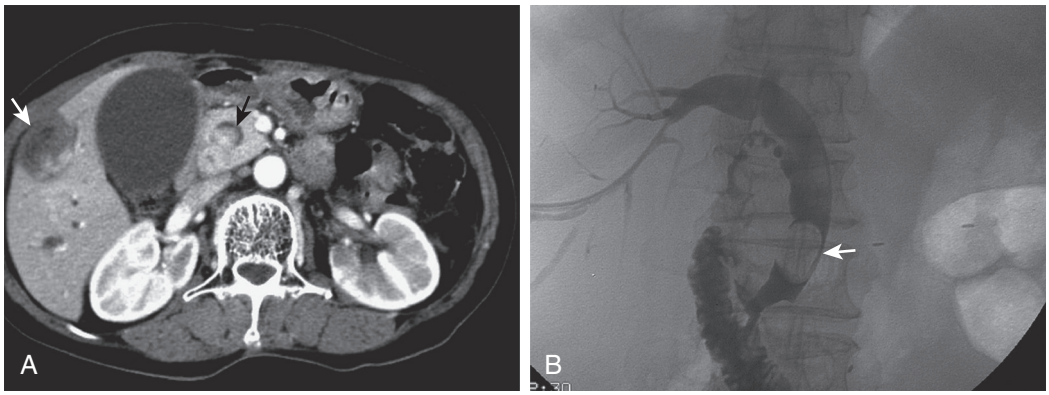

Figure 79-36 Leiomyosarcoma metastatic to the common hepatic duct. A. CT scan shows an enhancing polypoid tumor (*black arrow*) in dilated common bile duct. *White arrow* indicates a liver metastasis. **B.** Cholangiography shows an intraluminal mass (*arrow*) of the common bile duct.

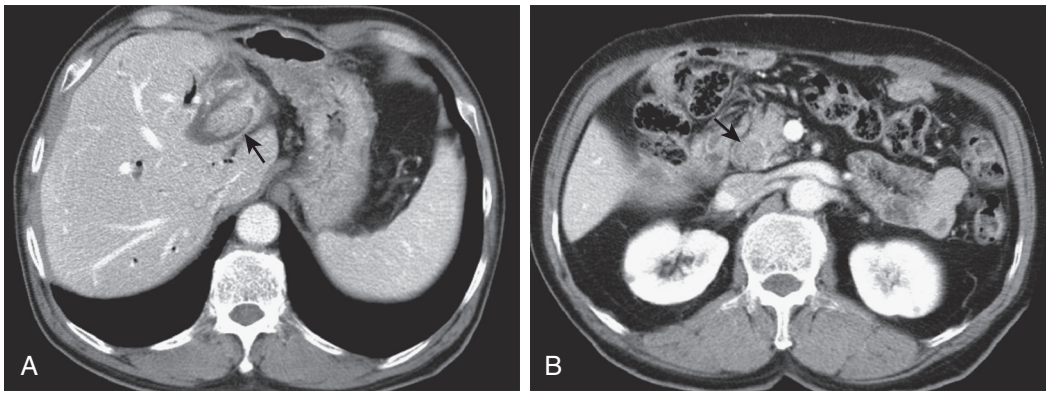

Figure 79-37 Multiple bile duct adenomas. A. Contrast-enhanced axial CT scan shows an intraluminal polypoid tumor (*arrow*) with homogeneous enhancement in dilated left intrahepatic bile duct. **B.** CT scan caudal to A demonstrates similar intraductal mass (*arrow*) in the common bile duct.

Benign Bile Duct Neoplasms

Benign neoplasms of the bile ducts are rare.[64] Adenomas are the most common type; others include granular cell tumors, hamartomas, fibromas, neuromas, lipomas, and heterotopic gastric or pancreatic mucosal rests.

Most adenomas are manifested as small asymptomatic polyps in the extrahepatic bile ducts that are found incidentally at surgery (Fig. 79-37). On occasion, they become large and cause biliary obstruction. Multiple papillary adenomas have been reported in association with obstructive biliary villous adenoma and ampullary carcinoma.[64,127,128] Granular cell tumors of the bile ducts occur most often in young African American women and cause abdominal pain and jaundice.[65] Most granular cell tumors are extrahepatic masses and are less than 3 cm in greatest dimension, and as the cell infiltrates the wall of the bile duct, the lumen is obliterated. CT and ultrasound usually show bile duct obstruction without identifying the mass. Cholangiography demonstrates either the extrahepatic bile ducts or a small polypoid mass.[64] Surgical resection is curative.

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