"Biliary Diseases with Pancreatic Counterparts": Cross-sectional Imaging Findings[1]

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On the basis of the similarities in the histopathologic findings and the clinical-biologic behaviors of select biliary and pancreatic conditions, a new disease concept, "biliary diseases with pancreatic counterparts," has been proposed. Both nonneoplastic and neoplastic pathologic conditions of the biliary tract have their counterparts in the pancreas. Immunoglobulin G4 (IgG4)–related sclerosing cholangitis is the biliary manifestation of IgG4-related sclerosing disease, and type 1 autoimmune pancreatitis is its pancreatic counterpart. People with chronic alcoholism can develop peribiliary cysts and fibrosis as well as pancreatic fibrosis and chronic pancreatitis simultaneously. Pancreatic ductal adenocarcinoma, intraductal papillary mucinous neoplasm, and mucinous cystic neoplasm are considered pancreatic counterparts for the biliary neoplasms of extrahepatic cholangiocarcinoma, intraductal papillary neoplasm of the biliary tract, and hepatic mucinous cystic neoplasm, respectively. The anatomic proximity of the biliary tract and the pancreas, the nearly simultaneous development of both organs from the endoderm of the foregut, and the presence of pancreatic exocrine acini within the peribiliary glands surrounding the extrahepatic bile ducts are suggested as causative factors for these similarities. Interestingly, these diseases show "nearly" identical findings at cross-sectional imaging, an observation that further supports this new disease concept. New information obtained with regard to biliary diseases can be used for evaluation of pancreatic abnormalities, and vice versa. In addition, combined genetic and molecular studies may be performed to develop novel therapeutic targets. For both biliary and pancreatic diseases, imaging plays a pivotal role in initial diagnosis, evaluation of treatment response, efficacy testing of novel drugs, and long-term surveillance.

Abbreviations: H-E = hematoxylin-eosin, IgG4 = immunoglobulin G4

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SA-CME LEARNING OBJECTIVES

After completing this journal-based SA-CME activity, participants will be able to:

- Discuss the newly proposed disease concept, "biliary diseases with pancreatic counterparts."
- List select inflammatory and neoplastic diseases of the bile ducts that have pancreatic counterparts, and discuss evolving concepts with regard to their pathogenesis.
- Describe similarities between cross-sectional imaging findings of these biliary and pancreatic diseases, and correlate with the histopathologic findings.

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Introduction

Select inflammatory and neoplastic diseases affecting the biliary tract demonstrate similar pathogenesis, histopathologic and immunohistochemical findings, clinical features, and biologic behavior to those of some pancreatic conditions (1). Although exact reasons for these similarities remain to be fully clarified, efforts are under way to explain them in a reasonable way on the basis of observations of the anatomic, embryologic, and histopathologic characteristics of the

TEACHING POINTS

- On the basis of these similarities, a new disease concept, "biliary diseases with pancreatic counterparts," has been proposed by Nakanuma and colleagues. The nonneoplastic biliary diseases of immunoglobulin G4 (IgG4)–related sclerosing cholangitis and alcohol-induced peribiliary cysts and fibrosis have type 1 autoimmune pancreatitis and alcohol-related pancreatic fibrosis and chronic pancreatitis as their respective pancreatic counterparts. Biliary malignancies such as extrahepatic cholangiocarcinoma, intraductal papillary neoplasm of the biliary tract, and hepatic mucinous cystic neoplasm have pancreatic ductal adenocarcinoma, intraductal papillary mucinous neoplasm of the pancreas, and pancreatic mucinous cystic neoplasm as their respective pancreatic counterparts.
- Circumferential symmetric wall thickening and progressive contrast enhancement of the involved biliary ducts in IgG4-related sclerosing cholangitis compare well to progressive delayed enhancement of the peripancreatic "rimlike" soft-tissue thickening in patients with type 1 autoimmune pancreatitis.
- Extrahepatic cholangiocarcinoma and pancreatic ductal adenocarcinoma share many cross-sectional imaging features, in large part because of the abundant fibrous stroma found in both neoplasms. Extrahepatic cholangiocarcinoma is usually iso- to hypointense on T1-weighted MR images and centrally hypointense with a rim of hyperintensity on T2-weighted MR images; pancreatic ductal adenocarcinoma demonstrates hypointensity on both T1- and T2-weighted MR images. Both tumors show hypoenhancement in relation to the background biliary and pancreatic parenchyma in the early arterial phase at dynamic contrast-enhanced CT and MR imaging, with progressive enhancement in the portal venous and delayed phases.
- Biliary cystic tumors such as biliary cystadenoma and cystadenocarcinoma that show definite communication with the adjacent bile ducts are now regarded as cystic intraductal papillary neoplasms of the biliary tract; a prominent cystic dilatation of the bile duct and mucin retention are the cause for cyst formation, rather than a true cystic neoplasm.
- Mucinous cystic neoplasm of the liver is a cyst-forming biliary epithelial neoplasm composed of mucin-producing epithelium and characterized by ovarian-like stroma; this neoplasm is a distinct entity that differs clinically, histopathologically, and radiologically from cystic intraductal papillary neoplasm of the biliary tract.

biliary tract and pancreas. The extrahepatic biliary ducts and a portion of the pancreas develop from the endoderm of the foregut simultaneously during fetal life. In addition, the biliary tract and pancreas lie in anatomic proximity to each other (1,2). Moreover, biliary ductal and pancreatic ductal epithelia show similar morphologic structures and phenotypes because both are accompanied by periductal glands; there are remnants of pancreatic exocrine acini within the peribiliary glands surrounding the biliary tract (1).

On the basis of these similarities, a new disease concept, "biliary diseases with pancreatic counterparts," has been proposed by Nakanuma and colleagues (2). The nonneoplastic biliary diseases of immunoglobulin G4 (IgG4)–related sclerosing cholangitis and alcohol-induced peribiliary cysts and fibrosis have type 1 autoimmune pancreatitis and alcohol-related pancreatic fibrosis and chronic pancreatitis as their respective pancreatic counterparts. Biliary malignancies such as extrahepatic cholangiocarcinoma, intraductal papillary neoplasm of the biliary tract, and hepatic mucinous cystic neoplasm have pancreatic ductal adenocarcinoma, intraductal papillary mucinous neoplasm of the pancreas, and pancreatic mucinous cystic neoplasm as their respective pancreatic counterparts (Table) (1,2). Interestingly, these biliary diseases demonstrate somewhat similar imaging findings to those of their pancreatic counterparts at computed tomography (CT) and magnetic resonance (MR) imaging; this similarity can provide further supporting evidence for this novel disease concept. In addition, correlation between imaging findings and histopathologic features plays an important role in the detailed evaluation of these pathologic conditions. Imaging also can be used to assist in testing the efficacy of new drugs and in long-term surveillance (3).

The purpose of this article is to examine the relationship between certain biliary diseases and their pancreatic counterparts, to explore the proposed new disease concept—biliary diseases with pancreatic counterparts. First, the anatomic structure and embryologic development of the biliary tract and the pancreas are described, with special emphasis on the peribiliary glands. Then the clinical, histopathologic, and imaging similarities between select biliary diseases and their pancreatic counterparts are reviewed. Finally, future clinical implications of this disease concept are discussed, as well as how imaging studies could be helpful in future research and, ultimately, in patient care.

Anatomy and Embryology: Pancreaticobiliary Tree and the Peribiliary Glands

The biliary system consists of the gallbladder and the intrahepatic and extrahepatic bile ducts. The extrahepatic bile ducts consist of the right, left, and common hepatic ducts, the common bile duct, and the cystic duct. The common bile duct joins the main pancreatic duct at the ampulla of Vater to drain into the duodenum. The epithelial linings of the biliary tract and of the main pancreatic duct demonstrate similar histologic findings (columnar epithelium), immunohistochemical phenotypes (expression of cytokeratins 7 and 19), and metaplastic change (intestinal, gastric, and oncocytic) (4).

In addition, there are glandular elements that accompany the biliary tract (peribiliary glands) and the pancreatic duct (pancreatic periductal glands). The extrahepatic and large intrahepatic

Biliary Diseases with Pancreatic Counterparts

Type of Biliary Disease	Pancreatic Counterpart
Inflammatory disease	
IgG4-related sclerosing cholangitis	Type 1 autoimmune pancreatitis
Peribiliary cysts in subjects with alcoholism	Chronic pancreatitis in subjects with alcoholism
Neoplastic disease	
Extrahepatic cholangiocarcinoma	Pancreatic ductal adenocarcinoma
Intraductal papillary neoplasm of the biliary tract	Intraductal papillary mucinous neoplasm of the pancreas
Hepatic mucinous cystic neoplasm	Pancreatic mucinous cystic neoplasm

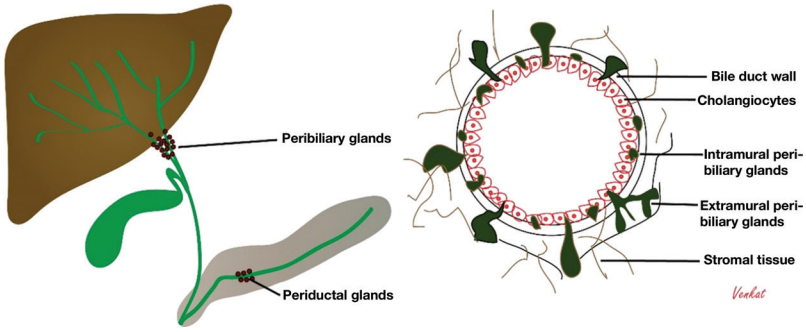
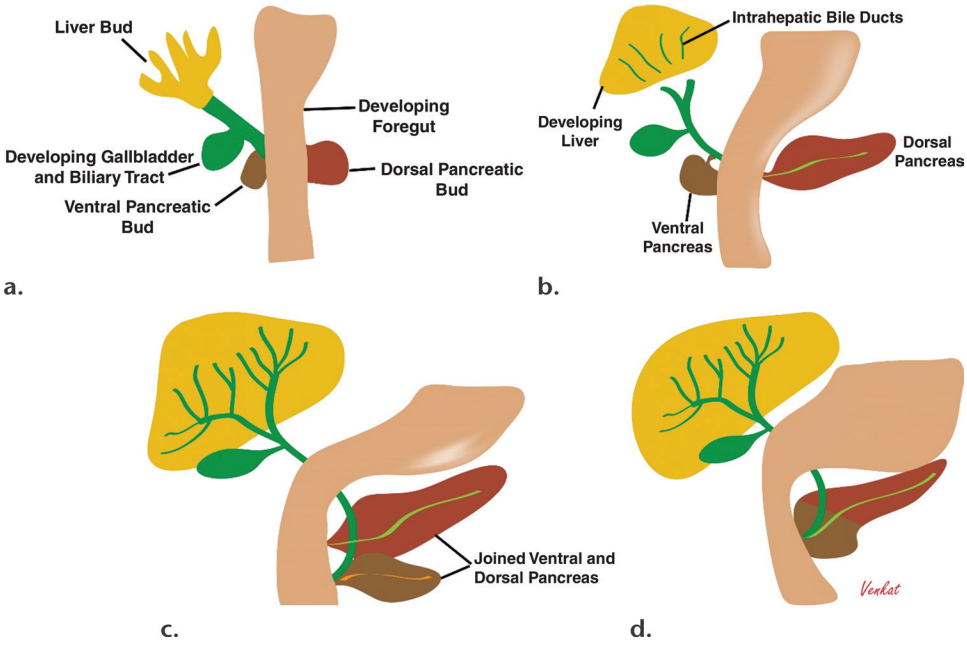


Figure 1. Normal pancreaticobiliary anatomic structures, with emphasis on the peribiliary glands. Left: Drawing of the normal anatomic structures of the pancreaticobiliary system shows the peribiliary glands surrounding the extrahepatic and large intrahepatic bile ducts and the periductal glands around the main pancreatic duct. Right: Drawing shows a cross section of a segment of the extrahepatic bile duct containing both intra- and extramural peribiliary glands.

bile ducts are surrounded by peribiliary glands that drain their secretions into the bile. Thus, the biliary tract acts as a conduit for the secretions from the hepatic parenchyma (bile) and from the peribiliary glands. The peribiliary glands can be located within the bile duct wall (intramural type) or the periductal connective tissue (extramural type) (Fig 1) (5,6). Although intramural peribiliary glands are simple tubular mucous glands, extramural peribiliary glands are branched tubuloalveolar seromucous glands. The functions of the peribiliary glands are to *(a)* secrete mucus for lubrication of the bile stream, *(b)* concentrate bile, and *(c)* protect the mucosal surface by secreting immunoglobulins (1). Not only are there scattered pancreatic exocrine acini that infrequently admix with the extramural peribiliary glands, but also pancreatic enzymes such as α-amylase, lipase, and trypsin are immunochemically detected within the peribiliary glands (7). In addition, the peribiliary glands are reservoirs for pluripotent stem (progenitor) cells that can differentiate into hepatocytes, cholangiocytes, and pancreatic cells, depending on the microenvironment (8). On the basis of the histopathologic and immunohistochemical findings, it has been shown that the peribiliary glands can be considered as important players in the normal physiologic function as well as the pathogenesis of select inflammatory and neoplastic biliary diseases (1,5,6).

Although the extrahepatic bile ducts arise from the endoderm of the foregut in conjunction with the ventral pancreas simultaneously, the intrahepatic bile ducts develop from the ductal plate along with the hepatocytes within the liver bud (Fig 2) (9–11). The ventral pancreas rotates to join with the dorsal pancreas, and the extrahepatic biliary ducts continue to grow and join with the intrahepatic ducts, giving rise to the entire pancreaticobiliary system (11). The biliary tract and the pancreas demonstrate plasticity during embryologic development. Multiple cell signaling pathways govern the orderly development of pancreatic epithelium and biliary epithelium from the common progenitor cells; transcription factors such as pancreatic duodenal homeobox factor 1 (Pdx1) and hairy enhancer of split-1 (Hes1) are critically involved in this process (10,12). Pdx1-positive progenitor cells develop into the pancreatic epithelium, whereas Pdx1-negative cells give rise to the biliary epithelium; this process is also supported by other proteins, including Neurog3, Notch, Sox17, Sox9, and hepatocyte nuclear factor 6 (13). Any abnormality in expression of the genes associated with these proteins may lead to the acquisition of pancreatic features or the presence of pancreatic remnants within the biliary epithelium; this abnormality may be potentially responsible for the pathogenesis of several biliary diseases,

Figure 2. Development of the pancreas and biliary system. These four drawings show the sequential development of the extrahepatic bile ducts and the ventral pancreatic bud from the foregut almost at the same time. This similar timing could be the reason for the remnants of pancreatic exocrine acini within the bile duct wall. **(a)** Drawing shows that the ventral pancreatic bud and the extrahepatic biliary tree arise from the ventral aspect of the developing foregut together at the same time. **(b)** Drawing shows the growth of the ventral pancreas, dorsal pancreas, extrahepatic bile ducts, and gallbladder. The liver and intrahepatic bile ducts develop together from the liver bud. **(c)** Drawing shows the rotation of the ventral pancreas to join with its dorsal counterpart, as well as the growth of the gallbladder and growth of the extrahepatic bile ducts to join with the intrahepatic bile ducts and finally form the biliary system. **(d)** Drawing shows the completely developed pancreaticobiliary system.



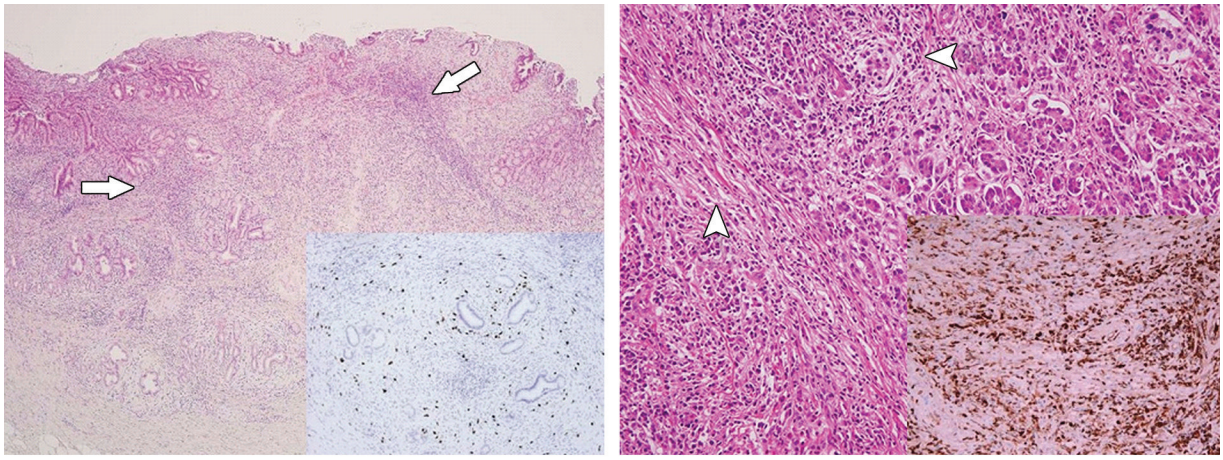
especially neoplastic conditions with multiple genetic and epigenetic alterations (12). Given *(a)* the close embryologic and anatomic relationship of the biliary tree and the pancreas, *(b)* the presence of pancreatic acini within the peribiliary glands, and *(c)* the ability of the biliary tract to differentiate into the pancreas when there are abnormalities in the cell signaling pathways, the biliary tract can be considered as an "incomplete pancreas" (1). This theory helps explain the clinical and histopathologic similarities between biliary and pancreatic diseases.

Inflammatory Diseases

IgG4-related Sclerosing Cholangitis and Type 1 Autoimmune Pancreatitis

IgG4-related sclerosing cholangitis and type 1 autoimmune pancreatitis are biliary and pancreatic manifestations, respectively, of the spectrum of a unique recently described clinical entity known as IgG4-related disease; more than 90% of patients with IgG4-related sclerosing cholangitis have type 1 autoimmune pancreatitis, and about 60%–80% of patients with type 1 autoimmune pancreatitis have associated IgG4-related sclerosing cholangitis (14,15). Both type 1 autoimmune pancreatitis and IgG4-related sclerosing cholangitis share several clinical similarities and often manifest together. Both diseases are seen more commonly in middle-aged to elderly men and often manifest with obstructive jaundice, and affected patients have elevated serum γ-globulin and IgG4 levels (16,17).

Although the exact pathogenetic mechanisms of IgG4-related sclerosing cholangitis and type 1 autoimmune pancreatitis are still unclear, autoimmune reaction to common "antigens" inherent to the biliary tract and pancreas has been suspected; abnormal innate immunity, activation of the complement system, and regulatory T cells and B cells may play a role in pathogenesis (15). Some antigens or enzymes located in pancreatic acini could be the target of immunologic attack, given the severe damage of the peribiliary glands that contain small amounts of pancreatic exocrine acini in patients with IgG4-related sclerosing cholangitis and the substantial damage and atrophy of exocrine acini within the pancreas in patients with type 1 autoimmune pancreatitis (1,18). At gross pathologic examination, the affected bile ducts in IgG4-related sclerosing cholangitis appear whitish and fleshy and show diffuse and circumferential thickening of the wall with sharp margins against the liver parenchyma, whereas in type 1 autoimmune pancreatitis, the affected portion of the



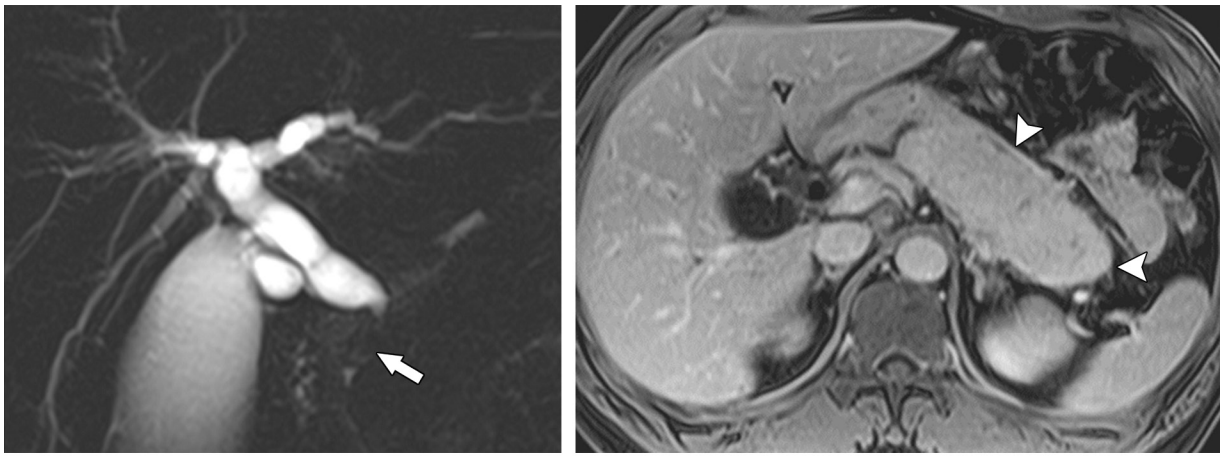
a. b.

Figure 3. Histopathologic findings of IgG4-related sclerosing cholangitis **(a)** and type 1 autoimmune pancreatitis **(b)**. **(a)** Low-power photomicrograph of IgG4-related sclerosing cholangitis in a 42-year-old woman shows inflammatory cell infiltration and fibrosis of the bile duct wall (arrows); note that the inflammatory cell infiltration is more intense on the luminal side. (Hematoxylin-eosin [H-E] stain; original magnification, ×40.) Inset: Photomicrograph shows strong staining of inflammatory cells with IgG4 immunohistochemical stain. (Original magnification, ×200.) **(b)** Low-power photomicrograph of type 1 autoimmune pancreatitis in a 49-year-old man shows multiple inflammatory cells interspersed with areas of storiform fibrosis (arrowheads). (H-E stain; original magnification, ×100.) Inset: Photomicrograph shows strong reactivity to IgG4 immunohistochemical stain. (Original magnification, ×200.)

pancreas demonstrates gray to yellowish white induration with loss of the normal lobular structure (19,20). Both IgG4-related sclerosing cholangitis and type 1 autoimmune pancreatitis are histologically characterized by marked lymphoplasmacytic infiltration, abundant IgG4-positive plasma cells, irregular storiform fibrosis, and obliterative phlebitis (Fig 3) (21,22). In IgG4-related sclerosing cholangitis, the inflammatory infiltrate and fibrosis are largely found in the submucosa of the biliary wall, with relative sparing of the epithelial lining, but result in severe damage to the peribiliary glands (19). In type 1 autoimmune pancreatitis, periductal lymphoplasmacytic infiltrate surrounds many small-sized ducts and results in swirling storiform fibrosis centered around the ducts and veins (20).

Given the considerable overlap in the pathogenesis and histopathologic findings of IgG4-related sclerosing cholangitis and type 1 autoimmune pancreatitis, some similarities at imaging may be expected. Concentric duct wall thickening, delayed enhancement after contrast material administration, and multiple strictures are the common imaging manifestations of IgG4-related sclerosing cholangitis and type 1 autoimmune pancreatitis. However, because of the larger caliber of the bile ducts, the ductal manifestations are more prominent with IgG4-related sclerosing cholangitis, and parenchymal manifestations predominate in type 1 autoimmune pancreatitis (23). However, there are some similarities between IgG4-related sclerosing cholangitis and type 1 autoimmune pancreatitis that can be identified at cross-sectional imaging. Simultaneous manifestations of both pathologic conditions in the same patient can be easily identified with CT or MR imaging (Fig 4). Circumferential symmetric wall thickening and progressive contrast enhancement of the involved biliary ducts in IgG4-related sclerosing cholangitis compare well to progressive delayed enhancement of the peripancreatic "rimlike" soft-tissue thickening in patients with type 1 autoimmune pancreatitis (Fig 5) (23,24). Substantial periductal and peripancreatic fibrosis may be responsible for these findings. Wall thickening of a short segment of the bile duct with upstream biliary ductal dilatation in IgG4-related sclerosing cholangitis mimics the periductal type of cholangiocarcinoma, whereas a focal form of type 1 autoimmune pancreatitis with minimal associated pancreatic ductal dilatation simulates pancreatic adenocarcinoma (Fig 6). Histologically, a focal collection of inflammatory cells with associated fibrosis, a finding seen in both conditions, could be the potential reason for this appearance (1). In IgG4-related sclerosing cholangitis, focal or multifocal biliary strictures are most commonly seen in the distal common bile duct and hilar and central intrahepatic bile ducts. This imaging feature correlates with the abundance of peribiliary glands in these locations at histopathologic examination (5). Patients with type 1 autoimmune pancreatitis may also occasionally demonstrate focal or multifocal pancreatic ductal strictures, ectatic side branches arising from the site of the stricture, and a lack of upstream ductal dilatation (25,26).

The response to corticosteroid therapy is a characteristic feature of both IgG4-related



a. b.

Figure 4. Simultaneous occurrence of IgG4-related sclerosing cholangitis and type 1 autoimmune pancreatitis in a 42-year-old man. **(a)** Coronal T2-weighted MR cholangiopancreatographic image shows short-segment stricture (arrow) of the distal common bile duct, with upstream biliary ductal dilatation. **(b)** Axial contrast-enhanced T1-weighted MR image (portal venous phase) obtained after administration of gadolinium-based contrast material shows a sausage-shaped pancreas with an enhancing peripancreatic soft-tissue rim (arrowheads), findings consistent with type 1 autoimmune pancreatitis.

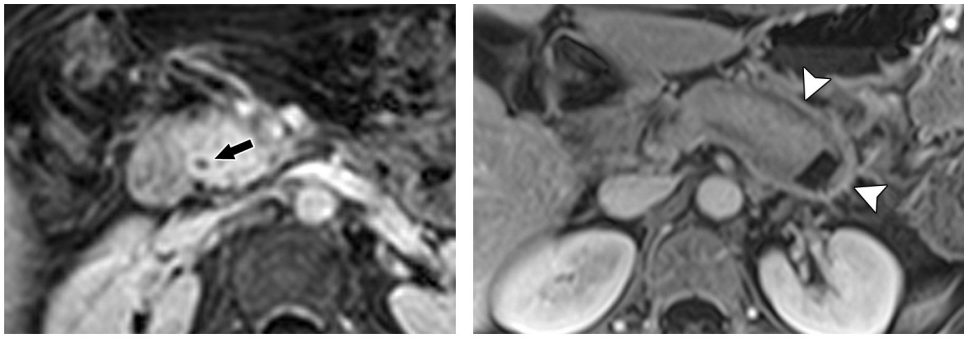


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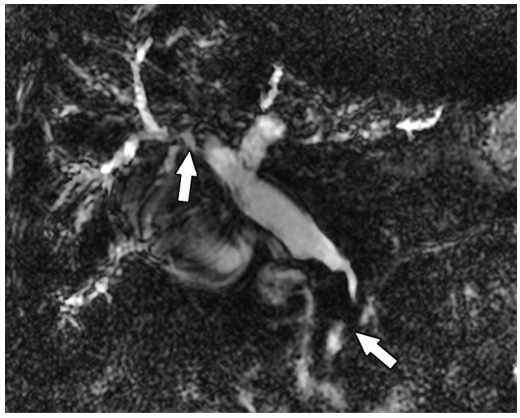
Figure 5. Imaging similarities between IgG4-related sclerosing cholangitis and type 1 autoimmune pancreatitis. **(a)** Axial contrast-enhanced T1-weighted MR image (portal venous phase) depicts enhancement of the narrowed segment of the common bile duct (arrow) in this 57-year-old man with known IgG4-related sclerosing cholangitis. **(b)** Axial contrast-enhanced T1-weighted MR image (portal venous phase) shows enhancement of the peripancreatic soft-tissue rim (arrowheads) in a 47-year-old man with type 1 autoimmune pancreatitis. The presence of appreciable fibrosis in both pathologic conditions is thought to be the cause for these findings.

sclerosing cholangitis and type 1 autoimmune pancreatitis and corroborates the diagnosis. An extensive workup, including obtaining histologic samples, is essential to rule out alternate diagnoses. Cholangiocarcinoma and primary sclerosing cholangitis, in particular, should be ruled out before diagnosing IgG4-related sclerosing cholangitis; and pancreatic adenocarcinoma and lymphoma should be ruled out before confirming type 1 autoimmune pancreatitis (14). Patients whose condition does not respond to steroid therapy must be reevaluated to exclude malignancy; immunomodulators, as well as B-cell depleting agents such as rituximab, are alternate therapeutic options for steroid-refractory cases (14,15). The short-term prognosis is excellent for patients with IgG4-related sclerosing cholangitis and those with type 1 autoimmune pancreatitis; however, the long-term prognosis is not yet clearly known and can be influenced by several factors, including relapse, biliary cirrhosis, segmental or lobar hepatic atrophy, pancreatic exocrine or endocrine dysfunction, and associated malignancy (15,18,27).

Peribiliary Cysts and Chronic Pancreatitis in Patients with Alcoholism

Grossly visible perihilar cysts measuring as much as 1 cm are known as peribiliary cysts (2). They have been described in association with both congenital polycystic liver diseases and cirrhosis (16,28,29). Chronic alcoholic pancreatitis is a progressive inflammatory disease of the pancreas that eventually results in glandular atrophy



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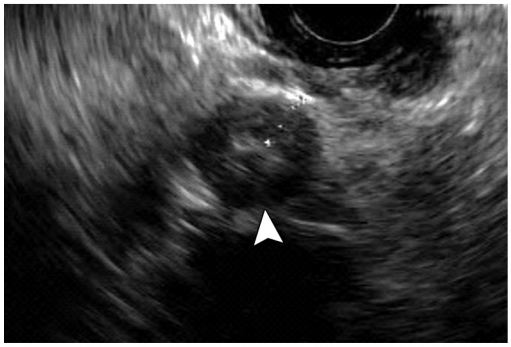

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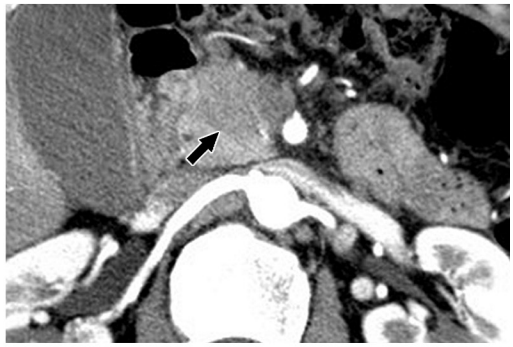
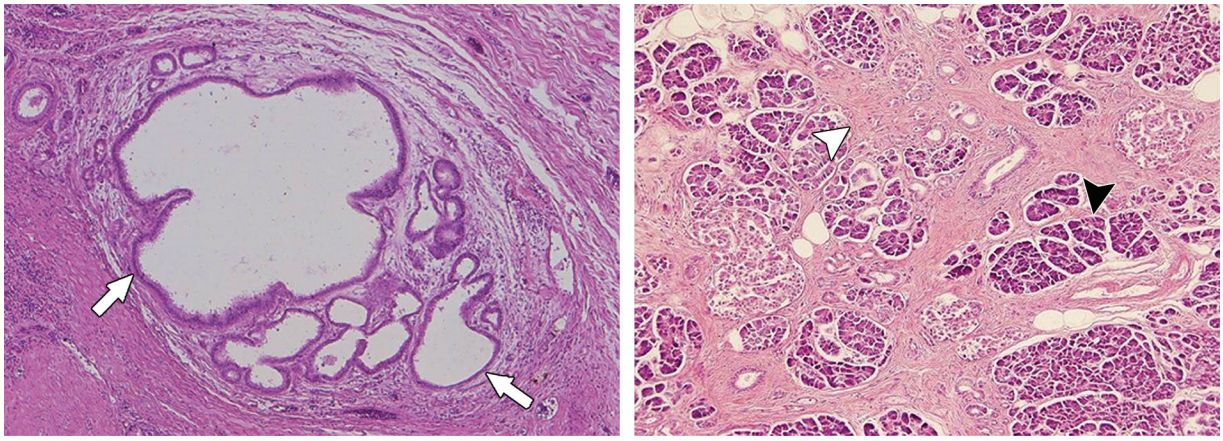


c.

Figure 6. IgG4-related sclerosing cholangitis and type 1 autoimmune pancreatitis mimicking cholangiocarcinoma and pancreatic ductal adenocarcinoma, respectively. **(a)** Coronal MR cholangiopancreatographic image of a 54-year-old man shows multifocal strictures (arrows) involving the intrahepatic bile ducts and the distal common bile duct. **(b)** Endoscopic ultrasonographic (US) image of the same 54-year-old man as in **a** shows irregular wall thickening (arrowhead) of a narrowed segment of the distal common bile duct, mimicking cholangiocarcinoma; the findings at histopathologic examination confirmed that this patient had IgG4-related sclerosing cholangitis. **(c)** Axial contrast-enhanced CT image of a 69-year-old woman shows an ill-defined area of hypoattenuation (arrow) in the head of the pancreas, a finding that raised concern for adenocarcinoma; however, the findings at histopathologic examination confirmed that this patient had type 1 autoimmune pancreatitis.

and fibrosis (30). A considerable number of the alcoholic patients with cirrhosis and chronic pancreatitis have peribiliary cysts, and it is suggested that alcoholic pancreatic or hepatic disease is frequently a background disease of peribiliary cysts (31). Progressive parenchymal fibrosis is a common denominator for chronic alcoholism–related pancreatic disease and hepatic disease with associated peribiliary cysts; alcoholic injuries to the pancreatic exocrine acini and the peribiliary glands may be followed by the development of progressive fibrosis in the former and adenitis, fibrosis, and cyst formation in the latter (31). In addition, activation of the hepatic stellate cells may also be related to fibrosis of the peribiliary glands and subsequent cyst formation (2). At histopathologic examination, adenitis and fibrosis of the peribiliary glands and associated peribiliary cysts have been shown to correlate closely with the extent of pancreatic fibrosis (Fig 7) (2,31).

At imaging, peribiliary cysts may appear as clusters of discrete cysts at the porta hepatis, a string of cysts simulating abnormal bile ducts, or a tubular structure paralleling the portal structures near the hepatic hilum (Fig 8) (28,32). Peribiliary cysts are typically anechoic at US and demonstrate no visible color flow at color Doppler flow examination. At CT, peribiliary cysts demonstrate water attenuation without any contrast enhancement (28). At MR imaging, peribiliary cysts are hyperintense on T2-weighted and hypointense on T1-weighted MR images, without any identifiable enhancement after administration of gadolinium-based contrast material (Fig 9) (32). The common imaging features of chronic pancreatitis are atrophic pancreatic parenchyma with irregular dilatation of the main pancreatic duct and its branches, as well as coarse parenchymal calcifications (Fig 8) (33). It is important to differentiate peribiliary cysts from dilated bile ducts, periportal edema, cystic neoplasms, and abscess to avoid unnecessary imaging and interventions. Additionally, the presence of peribiliary cysts at imaging should



a. b.

Figure 7. Histopathologic findings of peribiliary cysts **(a)** and chronic pancreatitis **(b)**. **(a)** High-power photomicrograph of a 73-year-old man shows microcystic dilatation of the peribiliary glands (arrows) with associated edema and inflammatory cell infiltration, findings consistent with adenitis. (H-E stain; original magnification, ×100.) **(b)** High-power photomicrograph of an 81-year-old man shows scattered areas of fibrosis interspersed with pancreatic acini (arrowheads), findings consistent with chronic pancreatitis. (H-E stain; original magnification, ×100.)

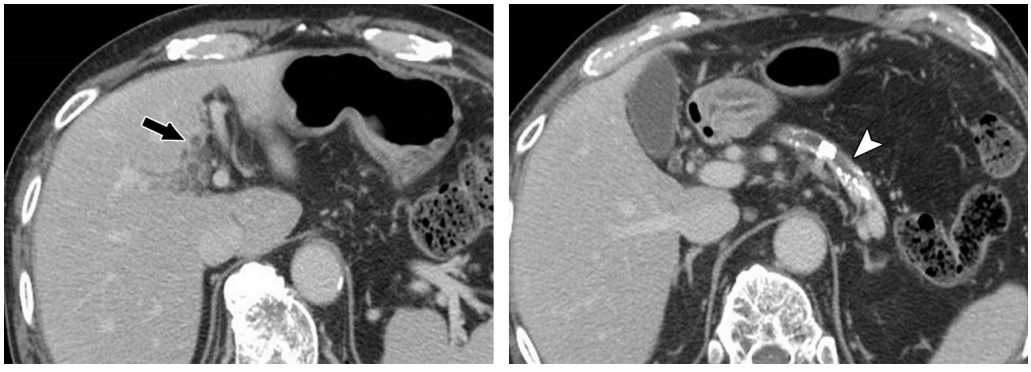


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Figure 8. Simultaneous occurrence of peribiliary cysts **(a)** and chronic pancreatitis **(b)** in a 55-year-old alcoholic man. **(a)** Axial contrast-enhanced CT image depicts multiple small cysts (arrow) in the left perihilar area, a finding consistent with peribiliary cysts. **(b)** Axial contrast-enhanced CT image shows an atrophic pancreas with a dilated main pancreatic duct and calcifications (arrowhead), findings consistent with chronic pancreatitis.

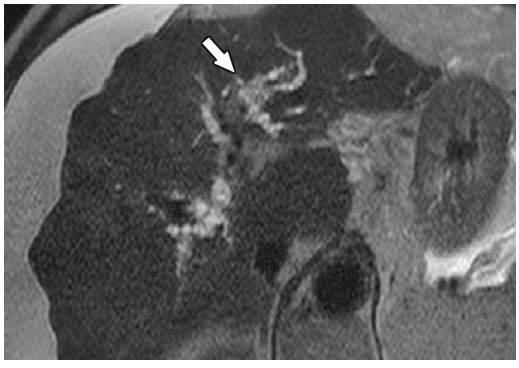


Figure 9. MR imaging findings of peribiliary cysts. Axial T2-weighted MR image of a 68-year-old alcoholic man shows cirrhotic morphologic structure of the liver with multiple hyperintense foci (arrow) along the perihilar bile ducts, findings consistent with peribiliary cysts. This same patient also had chronic pancreatitis (image not shown).

raise the suspicion of associated hepatic or pancreatic fibrosis, especially in subjects with alcoholism (Figs 8, 9) (28,32). The primary intervention in the management of alcoholic chronic pancreatitis and peribiliary cysts associated with cirrhosis is cessation of alcohol use.

Neoplastic Diseases

Extrahepatic Cholangiocarcinoma and Pancreatic Ductal Adenocarcinoma

Cholangiocarcinoma arising from the perihilar and distal bile ducts (extrahepatic cholangiocarcinoma) and pancreatic ductal adenocarcinoma are the most common malignancies arising from the bile ducts and from the pancreas, respectively. Both extrahepatic cholangiocarcinoma and pancreatic ductal adenocarcinoma

are clinically aggressive neoplasms that show similar pathogenesis, histopathologic features, and clinical-biologic behaviors; thus, pancreatic ductal adenocarcinoma can be considered as the pancreatic counterpart of extrahepatic cholangiocarcinoma (34). In both malignancies, patients typically present in their 6th and 7th decades of life with painless jaundice and usually already have an advanced stage of disease. Moreover, in both extrahepatic cholangiocarcinoma and pancreatic ductal adenocarcinoma, there is a slight male preponderance (35). In contrast, intrahepatic cholangiocarcinoma originates from small intrahepatic ducts that develop from the ductal plate along with the liver bud; currently, no histopathologic studies are available that compare this malignancy with pancreatic ductal adenocarcinoma.

At gross pathologic examination, extrahepatic cholangiocarcinoma and pancreatic ductal adenocarcinoma appear as firm grayish infiltrating masses that lack a capsule and demonstrate nodular-sclerosing growth features. At histopathologic examination, both malignancies *(a)* are typically well to moderately differentiated tubular adenocarcinomas with or without a micropapillary growth pattern, *(b)* produce mucin, and *(c)* have a high content of fibrotic stroma (Fig 10) (34,35). Additionally, perineural and lymphovascular invasion is common in both tumors. At immunohistochemical examination, both extrahepatic cholangiocarcinoma and pancreatic ductal adenocarcinoma stain positive for cytokeratin 7 (CK7), cytokeratin 20 (CK20), S100P protein, and anterior gradient protein 2; and there is strong expression of PDX1, HES1, MUC1, and MUC3 (Fig 10) (2,34). Further, it has been suggested that both extrahepatic cholangiocarcinoma and pancreatic ductal adenocarcinoma share, at least in part, a similar process of carcinogenesis; biliary intraepithelial neoplasia is considered as a preneoplastic lesion for extrahepatic cholangiocarcinoma, whereas pancreatic intraepithelial neoplasia is regarded as a precursor for pancreatic ductal adenocarcinoma (36). Both biliary intraepithelial neoplasia and pancreatic intraepithelial neoplasia show similar histopathologic findings and express PDX1, HES1, MUC1, MUC2, CK7, and CK20, suggesting similar phenotypic changes that result in progression to malignancy; and pancreatic intraepithelial neoplasia can be considered as the pancreatic counterpart of biliary intraepithelial neoplasia (Fig 10) (35,36). The lesions of pancreatic intraepithelial neoplasia develop from acinar cells that undergo acinar-ductal metaplasia; KRAS mutations and the Notch pathway promote initiation and progression of acinar-derived pancreatic intraepithelial neoplasms (2,36). In a similar fashion, it is speculated that the peribiliary glands containing exocrine pancreatic acini and biliary epithelia expressing pancreatic enzymes may be a source of development of biliary intraepithelial neoplasia (1,36).

Extrahepatic cholangiocarcinoma and pancreatic ductal adenocarcinoma share many cross-sectional imaging features, in large part because of the abundant fibrous stroma found in both neoplasms (37,38). Extrahepatic cholangiocarcinoma is usually iso- to hypointense on T1-weighted MR images and centrally hypointense with a rim of hyperintensity on T2-weighted MR images; pancreatic ductal adenocarcinoma demonstrates hypointensity on both T1- and T2-weighted MR images (38). Both tumors show hypoenhancement in relation to the background biliary and pancreatic parenchyma in the early arterial phase at dynamic contrast-enhanced CT and MR imaging, with progressive enhancement in the portal venous and delayed phases (Fig 11) (37–39). Additionally, extrahepatic cholangiocarcinoma and pancreatic ductal adenocarcinoma usually result in malignant ductal strictures, with associated upstream ductal dilatation. Vascular encasement and involvement of adjacent structures are common in both malignancies, findings that indicate the aggressive nature of these malignancies (Fig 12). Although both multidetector CT and MR imaging play important roles in determining the extent of disease, MR imaging with its superior soft-tissue resolution plays a useful role in staging and surgical planning, except in the evaluation of vascular involvement, where CT is more helpful.

Surgical resection and chemotherapy are the preferred management options for extrahepatic cholangiocarcinoma and pancreatic ductal adenocarcinoma. Because these malignancies commonly manifest at an advanced stage with local spread of disease and distant metastases, surgical cure is not usually a practical option. Moreover, these tumors are resistant to chemotherapy. Thus, the prognosis for both malignancies is grim, with a 5-year survival rate of about 2% for patients with extrahepatic cholangiocarcinoma and less than 5% for patients with pancreatic ductal adenocarcinoma (40).

Intraductal Papillary Neoplasm of the Biliary Tract and Intraductal Papillary Mucinous Neoplasm of the Pancreas

Intraductal papillary neoplasm of the biliary tract, a recently described distinct clinical and histopathologic entity, is defined as a biliary epithelial neoplasm with grossly visible papillary masses within the bile duct lumen that demonstrates predominantly an intraductal growth

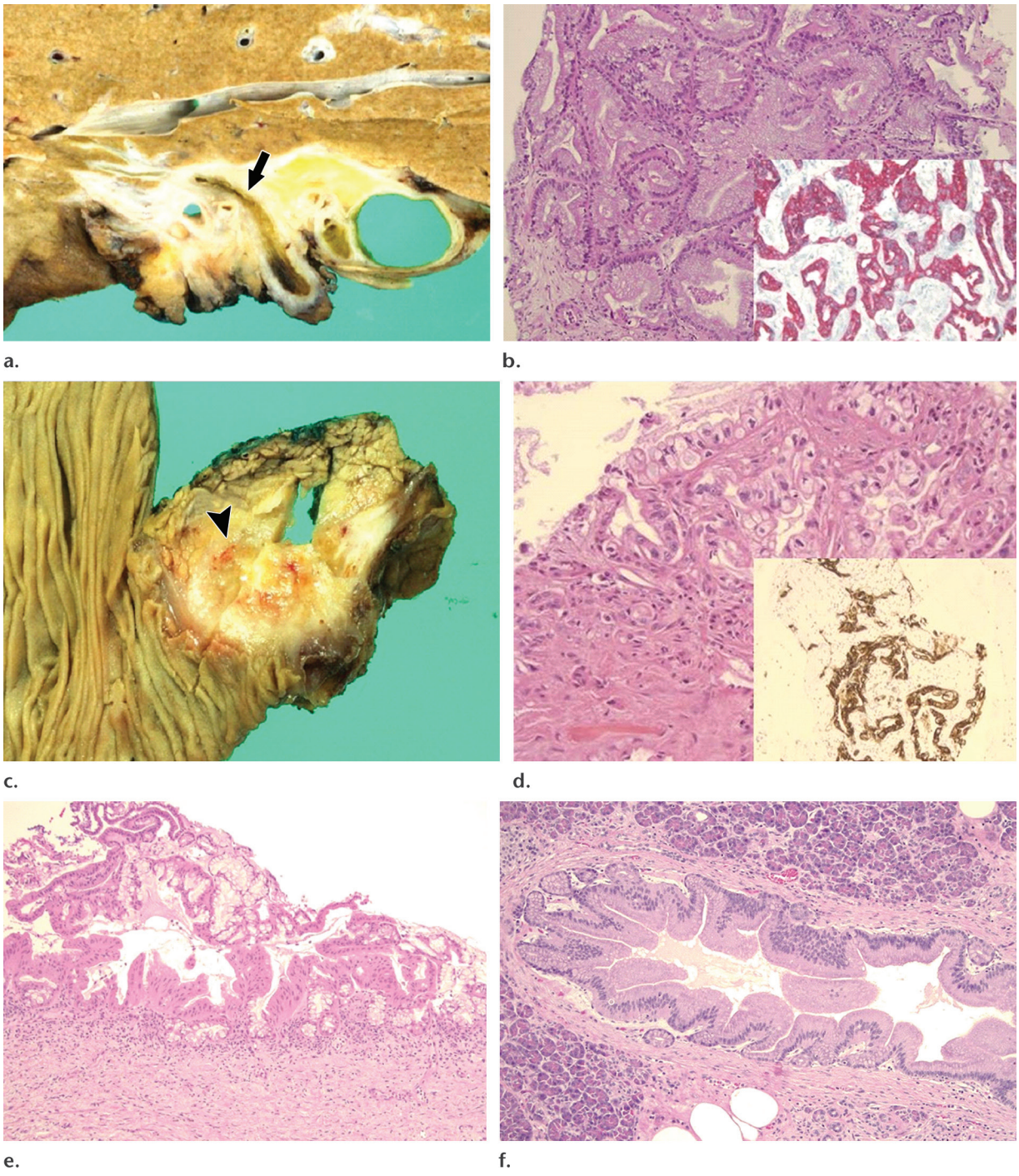


Figure 10. Histopathologic findings of pancreaticobiliary neoplastic diseases**. (a, b)** Extrahepatic cholangiocarcinoma in a 38-year-old woman. **(a)** Photograph of a cut section of the gross specimen shows diffuse irregular thickening of the hilar bile duct wall (arrow), with associated fibrosis and invasion. **(b)** High-power photomicrograph shows multiple small glands and tubules lined by low-grade malignant cells containing a considerable amount of mucin. (H-E stain; original magnification, ×200.) Inset: High-power photomicrograph shows strong reactivity to cytokeratin 7 immunohistochemical stain. (Original magnification, ×200.) **(c, d)** Pancreatic ductal adenocarcinoma in a 44-year-old woman. **(c)** Photograph of a cut section of the gross specimen shows a fibrotic mass (arrowhead) within the head of the pancreas, with focal areas of hemorrhage and necrosis. **(d)** High-power photomicrograph shows the highly invasive nature of small glands with increased pleomorphism and cytoplasmic clearing. (H-E stain; original magnification, ×200.) Inset: Photomicrograph shows strong reactivity to cytokeratin 7 immunohistochemical stain. (Original magnification, ×200.) **(e, f)** Precursor lesions of these two neoplastic diseases. **(e)** High-power photomicrograph of biliary intraepithelial neoplasia, the precursor lesion for extrahepatic cholangiocarcinoma, shows low-grade adenomatous changes within the bile duct epithelium, consisting of elongated cigar-shaped nuclei, foci of mucin, and eosinophilia. (H-E stain; original magnification, ×200.) **(f)** High-power photomicrograph of pancreatic intraepithelial neoplasia, the precursor lesion for pancreatic ductal adenocarcinoma, shows a histopathologic appearance similar to that of biliary intraepithelial neoplasia, consisting of low-grade adenomatous change with slightly elongated nuclei, eosinophilia, and foci of mucin. (H-E stain; original magnification, ×200.)

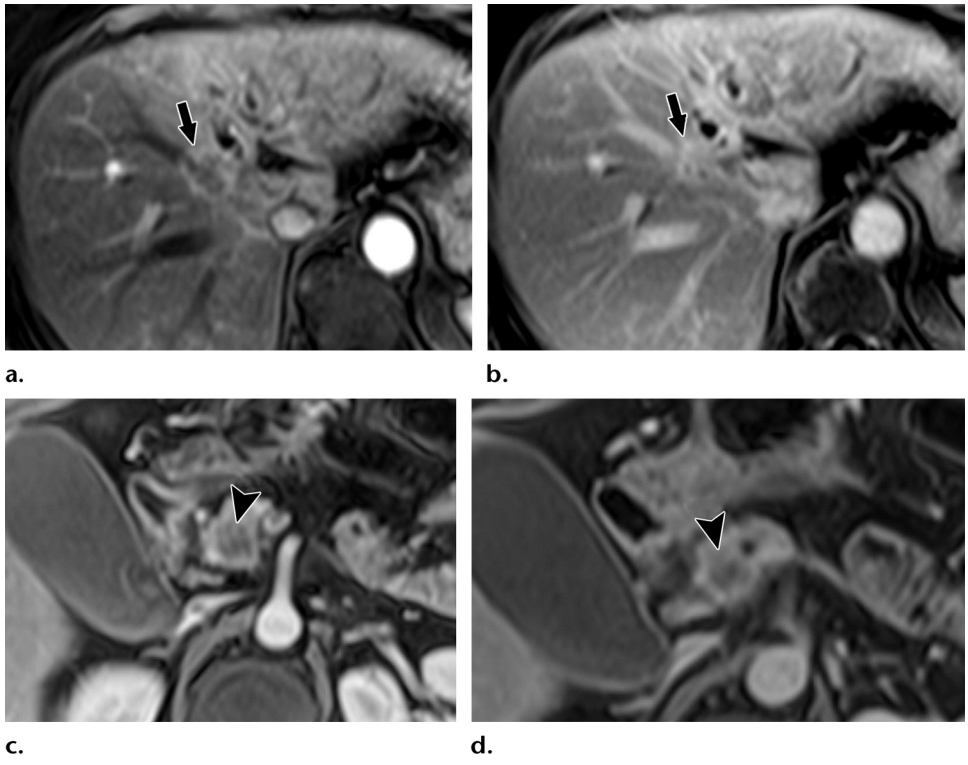


Figure 11. Imaging similarities between extrahepatic cholangiocarcinoma **(a, b)** and pancreatic ductal adenocarcinoma **(c, d)**. **(a, b)** Axial gadolinium-enhanced T1-weighted MR images of a 58-year-old man obtained during the arterial phase **(a)** and the portal venous phase **(b)** show an ill-defined mass (arrow) at the hepatic hilum, with heterogeneous peripheral enhancement during the arterial phase and progressive enhancement during the portal venous phase. **(c, d)** Axial gadolinium-enhanced T1-weighted MR images of an 82-year-old man obtained during the arterial phase **(c)** and the portal venous phase **(d)** show a mass (arrowhead) in the pancreatic head, with progressive contrast enhancement. The considerable amount of fibrotic tissue within both malignancies is likely the cause of the similarity in the imaging findings.

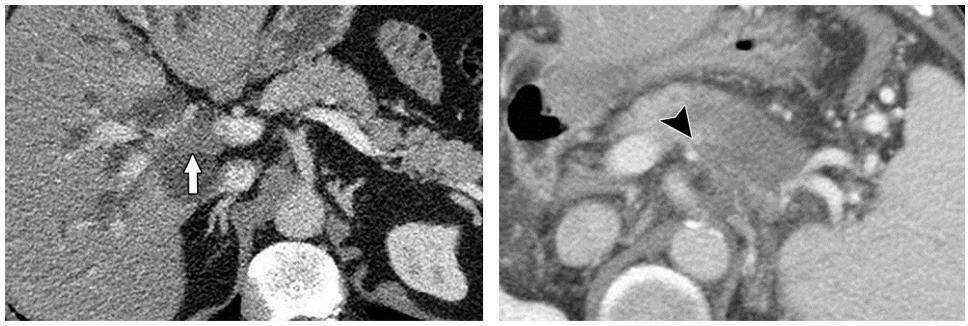


Figure 12. Appreciable vascular involvement in extrahepatic cholangiocarcinoma **(a)** and pancreatic ductal adenocarcinoma **(b)**. **(a)** Axial contrast-enhanced CT image of a 77-year-old man shows right portal vein encasement and narrowing by the hilar mass (arrow). **(b)** Axial contrast-enhanced CT image of a 65-year-old man depicts thrombosis of the splenic vein and artery secondary to encasement by the adjacent pancreatic adenocarcinoma (arrowhead).

pattern (41). Intraductal papillary neoplasm of the biliary tract includes biliary papilloma or papillomatosis, the intraductal growth type of cholangiocarcinoma, mucin-producing bile duct tumor, and papillary carcinoma of the biliary tract (42,43). Intraductal papillary neoplasms of the biliary tract are associated with a better prognosis compared with that for nonpapillary cholangiocarcinomas. On the basis of morphologic structure, intraductal papillary neoplasm of the biliary tract can be classified into three groups: duct-ectatic type, cystic type, and intermediate type. The duct-ectatic type is characterized by papillary tumors within a diffusely dilated duct. A cystic lesion with a communication with the intrahepatic bile duct

indicates a cystic type of intraductal papillary neoplasm of the biliary tract. The intermediate type is characterized by a cystic lesion containing a solid component that communicates with the dilated mucin-filled bile ducts (44). Biliary cystic tumors such as biliary cystadenoma and cystadenocarcinoma that show definite communication with the adjacent bile ducts are now regarded as cystic intraductal papillary neoplasms of the biliary tract; a prominent cystic dilatation of the bile duct and mucin retention are the cause for cyst formation, rather than a true cystic neoplasm (1,45). Intraductal papillary neoplasm of the biliary tract is currently considered as the "biliary" counterpart of intraductal papillary mucinous neoplasm of the pancreas on the basis of clinical and histopathologic findings (1,2,4,45,46). Main duct, branch duct, and mixed intraductal papillary mucinous neoplasms of the pancreas are the pancreatic counterparts of duct-ectatic, cystic, and intermediate intraductal papillary neoplasms of the biliary tract, respectively (44). Intraductal papillary neoplasms of the biliary tract are typically found in patients from the Far East (Taiwan, Japan, and Korea), because of the high prevalence of hepatolithiasis and clonorchiasis, and commonly affect people in their 5th through 7th decades, with a variable sex preponderance. Right upper quadrant pain, recurrent cholangitis, obstructive jaundice, and anemia are common presenting symptoms of patients with intraductal papillary neoplasm of the biliary tract (47). In comparison, intraductal papillary mucinous neoplasm of the pancreas usually occurs in male patients in their 6th through 8th decades; and this finding can be incidental, or patients may present with abdominal pain, chronic pancreatitis, diabetes mellitus, or diarrhea (48).

The literature includes case reports of patients presenting with simultaneous occurrence of intraductal papillary neoplasm of the biliary tract and intraductal papillary mucinous neoplasm of the pancreas, which is suggestive of a common pathogenesis for both diseases (49,50). Intraductal papillary neoplasms of the biliary tract develop from biliary epithelium and progress through low-, intermediate-, and high-grade dysplasia to invasive carcinoma in a stepwise manner, which is similar to the pathogenesis of intraductal papillary mucinous neoplasm of the pancreas (41). Recently, it has been speculated that cystic intraductal papillary neoplasms of the biliary tract are, in fact, cystic and papillary neoplasms of the peribiliary glands, developing from exocrine pancreatic acini (51). At gross pathologic examination, duct-ectatic intraductal papillary neoplasm of the biliary tract and main duct intraductal papillary mucinous neoplasm of the pancreas demonstrate dilated ducts with a single or multiple polypoid masses that project into the lumen; in cystic intraductal papillary neoplasm of the biliary tract and branch duct intraductal papillary mucinous neoplasm of the pancreas, a multilocular cystic mass containing mucinous fluid and small polypoid masses is common. Although macroscopic mucin secretion is found in almost all intraductal papillary mucinous neoplasms of the pancreas, about only one-third of intraductal papillary neoplasms of the biliary tract contain visible mucus (Fig 13) (2,4). At histopathologic examination, both tumors show dilated ducts with intraductal papillary proliferations with fibrovascular cores lined by cuboidal to columnar neoplastic epithelial cells; interestingly, four phenotypic types of tumor cells are identified in both, including "intestinal," "gastric," "pancreaticobiliary," and "oncocytic" (Fig 13) (2,4). Of note, the pancreaticobiliary and intestinal types of tumor cells are more commonly associated with subsequent development of papillary adenocarcinoma. At immunohistochemical analysis, both tumors express MUC2, MUC5AC, and CK20 markers, and mutations of the KRAS gene are commonly identified at genetic analysis (1). Although there are similarities between intraductal papillary neoplasm of the biliary tract and intraductal papillary mucinous neoplasm of the pancreas, some important differences are also seen: Although the intestinal subtype is most common in intraductal papillary mucinous neoplasm of the pancreas, the pancreaticobiliary type is commonly seen in intraductal papillary neoplasms of the biliary tract. Also, mucin production is seen in almost all cases of intraductal papillary mucinous neoplasm of the pancreas, but only about one-third of cases of intraductal papillary neoplasms of the biliary tract demonstrate appreciable mucin production.

At CT or MR imaging, duct-ectatic intraductal papillary neoplasms of the biliary tract and main duct intraductal papillary mucinous neoplasms of the pancreas mimic each other and demonstrate intraductal masses and ductal dilatation as common imaging features (Fig 14) (44,52,53). At multidetector CT, duct-ectatic intraductal papillary neoplasms of the biliary tract show extensive tumor infiltration along the bile duct wall, in which the solid components enhance during the arterial phase and show washout in the delayed portal venous and delayed phases (52,54). Gadolinium-enhanced MR imaging with MR cholangiopancreatography is extremely helpful in the identification of

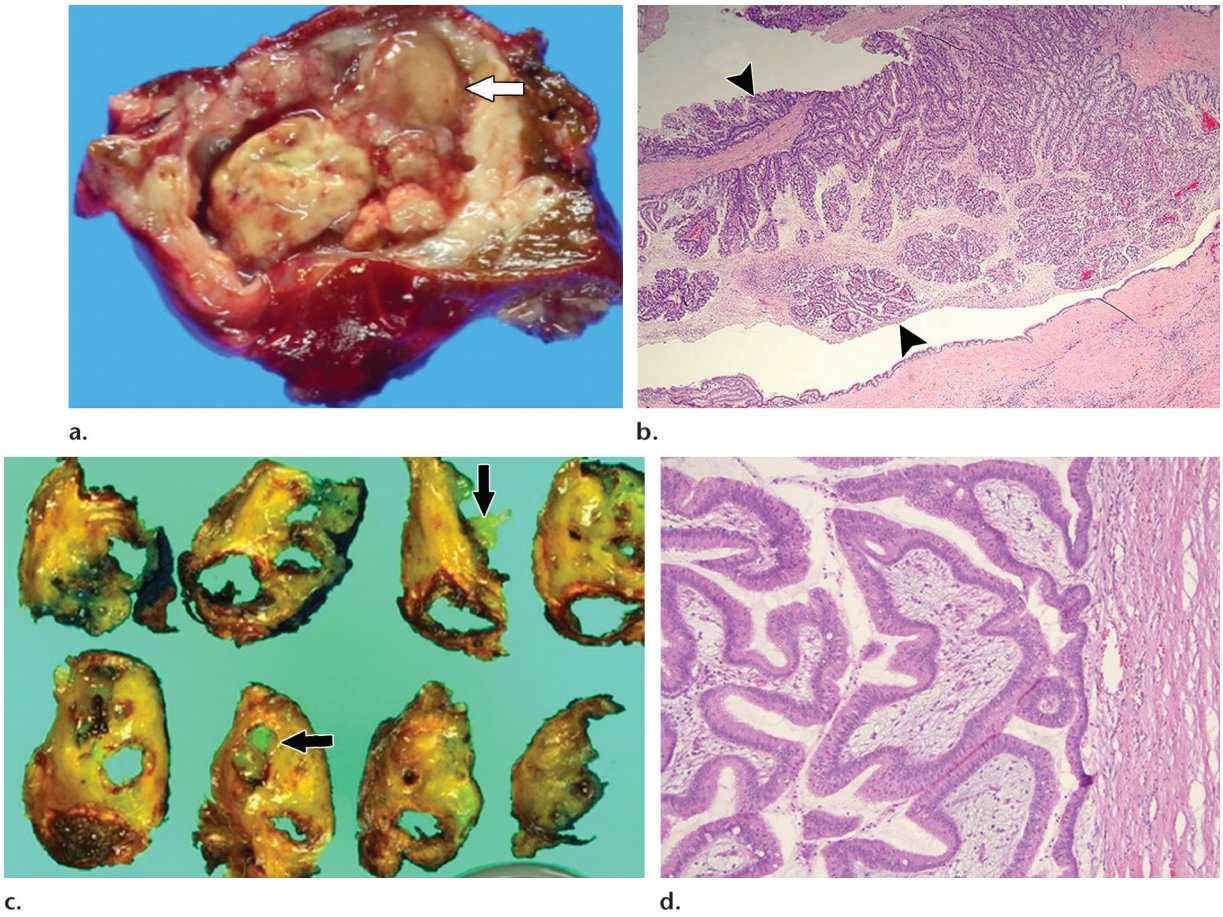
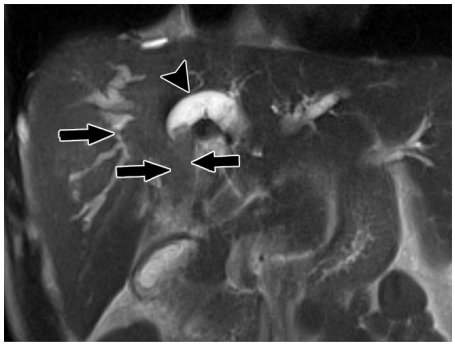


Figure 13. Histopathologic findings of intraductal papillary neoplasm of the biliary tract in a 44-year-old woman **(a, b)** and intraductal papillary mucinous neoplasm of the pancreas in a 75-year-old woman **(c, d)**. **(a)** Photograph of the gross specimen shows a considerably dilated bile duct filled with multiple solid masses and mucinous material (arrow). **(b)** High-power photomicrograph shows papillary growth of the gastric-type epithelium, with focal areas of invasive carcinoma in the cystically dilated bile duct (arrowheads), findings consistent with the gastric type of intraductal papillary neoplasm of the biliary tract. (H-E stain; original magnification, ×100.) **(c)** Photograph of multiple cut sections of the resected pancreas shows ductal dilatation with areas of mucin plugging (arrows) and a ragged appearance of the luminal mucosa that is due to papillae. **(d)** High-power photomicrograph shows papillary proliferation of low- to intermediate-grade intestinal-type epithelium, a finding consistent with the intestinal type of intraductal papillary mucinous neoplasm of the pancreas. (H-E stain; original magnification, ×200.)

tumor extension along the bile duct wall and intraductal tumors; the addition of diffusion-weighted MR imaging improves the conspicuity of intraductal tumors and is helpful in defining tumor invasiveness (Fig 14) (55). A markedly dilated main pancreatic duct with multiple visible papillary projections and polypoid masses is the most common imaging manifestation of main duct intraductal papillary mucinous neoplasm of the pancreas (Fig 14) (48,53). At endoscopic retrograde cholangiopancreatography, both of these tumors appear as dilated ducts with multiple intraluminal filling defects representing polypoid masses or mucin (Fig 15). In a similar fashion, the imaging features of cystic and intermediate intraductal papillary neoplasms of the biliary tract simulate branch duct and mixed intraductal papillary mucinous neoplasms of the pancreas, respectively (Fig 16) (53,56). Multilocular cystic masses with communicating intracystic spaces and multiple papillary nodules, with or without identifiable ductal communication, are the predominant imaging features in cystic intraductal papillary neoplasms of the biliary tract and branch duct intraductal papillary mucinous neoplasms of the pancreas (44,53,56). Intermediate intraductal papillary neoplasms of the biliary tract appear as multilocular cystic masses with a definite communication with a dilated bile duct (diverticulum-like appearance), and these findings are analogous to mixed intraductal papillary mucinous neoplasms of the pancreas (44,48). The presence of mural nodularity and the invasion of adjacent structures denote malignancy in both intraductal papillary neoplasms of the biliary tract and intraductal papillary mucinous neoplasms of the pancreas (47).

Surgical resection is the mainstay of treatment in intraductal papillary neoplasms of the



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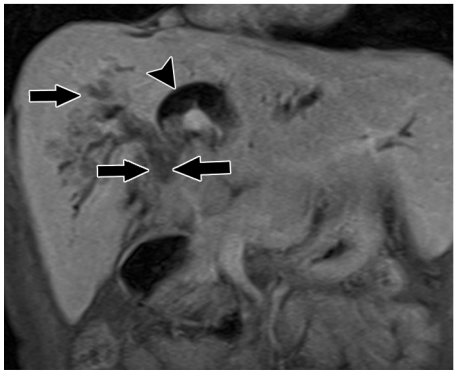

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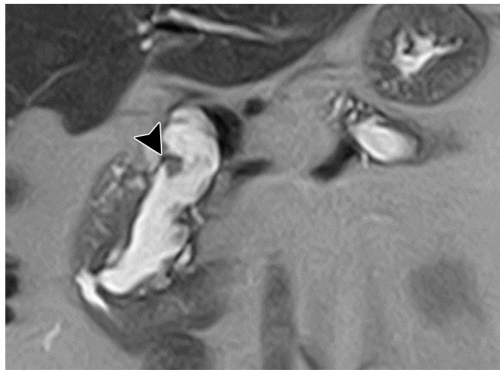


c.

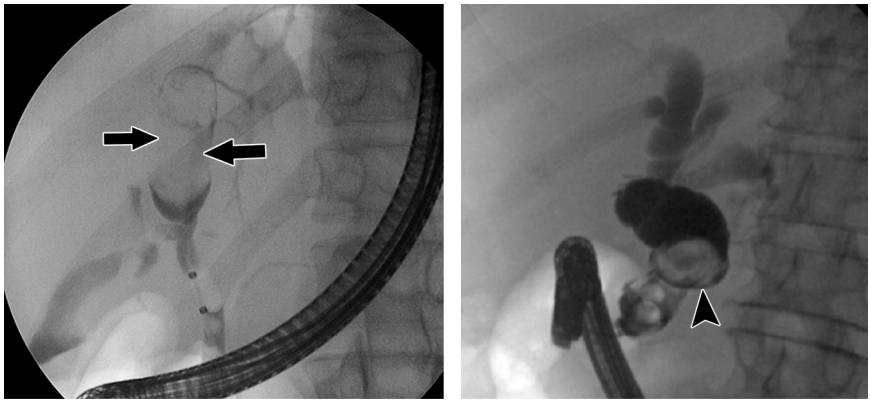
Figure 14. Imaging similarities between the duct-ectatic type of intraductal papillary neoplasm of the biliary tract **(a, b)** and the main duct type of intraductal papillary mucinous neoplasm of the pancreas **(c)**. **(a, b)** Coronal T2-weighted **(a)** and gadolinium-enhanced T1-weighted **(b)** MR images of a 56-year-old woman show an isointense minimally enhancing intraluminal mass within the common bile duct extending into the right and left intrahepatic bile ducts (arrows) with associated biliary ductal dilatation (arrowhead), findings consistent with the duct-ectatic type of intraductal papillary neoplasm of the biliary tract. **(c)** Coronal T2-weighted MR image of an 87-year-old man shows a dilated main pancreatic duct with multiple papillary projections (arrowhead) along the wall, findings consistent with the main duct type of intraductal papillary mucinous neoplasm of the pancreas.

biliary tract and intraductal papillary mucinous neoplasms of the pancreas; it has been shown that intraductal papillary neoplasms of the biliary tract carry a favorable prognosis, compared with that for nonpapillary cholangiocarcinomas (4). Similarly, intraductal papillary mucinous neoplasms of the pancreas show better treatment outcomes, in comparison with pancreatic ductal adenocarcinomas. Mucinous carcinomas developing from intraductal papillary neoplasms of the biliary tract and intraductal papillary mucinous neoplasms of the pancreas have more favorable prognoses than extrahepatic cholangiocarcinoma and pancreatic ductal adenocarcinoma (1).

Hepatic Mucinous Cystic Neoplasm and Pancreatic Mucinous Cystic Neoplasm

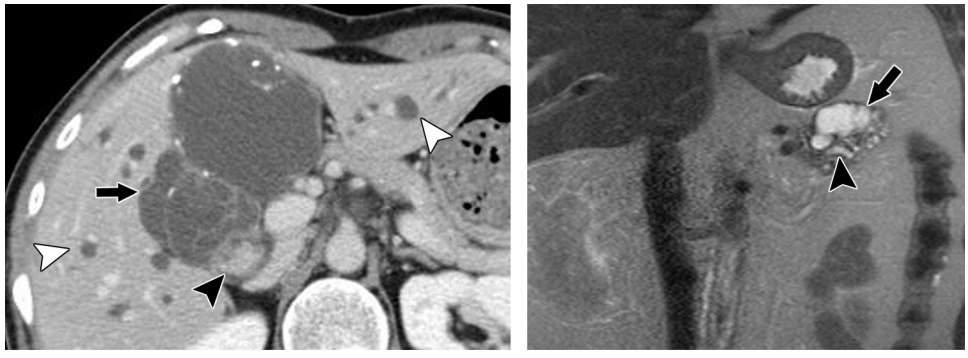
Mucinous cystic neoplasm of the liver is a cyst-forming biliary epithelial neoplasm composed of mucin-producing epithelium and characterized by ovarian-like stroma; this neoplasm is a distinct entity that differs clinically, histopathologically, and radiologically from cystic intraductal papillary neoplasm of the biliary tract (57,58). Pancreatic mucinous cystic neoplasm is also a cystic neoplasm characterized by ovarian-type stroma and mucin-secreting epithelium (59). Pancreatic mucinous cystic neoplasm is regarded as the pancreatic counterpart of mucinous cystic neoplasm of the liver (2,60). Both tumors occur almost exclusively in women, usually in the 4th–6th decades of life. Although these tumors may be asymptomatic, large masses may create a mass effect that results in a palpable mass, abdominal pain, nausea, and anorexia (59,60).

At gross pathologic examination, both lesions appear as multilocular cystic masses containing hemorrhagic fluid, with solid nodules along their walls. At histopathologic examination, both hepatic and pancreatic mucinous cystic neoplasms show columnar-type mucin-producing epithelium lining the wall, with dense cellular mesenchymal stroma that resembles ovarian stroma; thus, the embryologic origins may be related to germ cell migration early in fetal development (Fig 17) (4,59). Immunohistochemical analysis shows that both neoplasms express



a. b.

Figure 15. Endoscopic retrograde cholangiopancreatographic findings of intraductal papillary neoplasm of the biliary tract in a 56-year-old woman **(a)** and intraductal papillary mucinous neoplasm of the pancreas in a 73-year-old man **(b)**. Oblique endoscopic retrograde cholangiopancreatographic images show filling defects within the dilated common bile duct (arrows in **a**) and within the main pancreatic duct (arrowhead in **b**), findings consistent with duct-ectatic intraductal papillary neoplasm of the biliary tract and with the main duct type of intraductal papillary mucinous neoplasm of the pancreas, respectively.



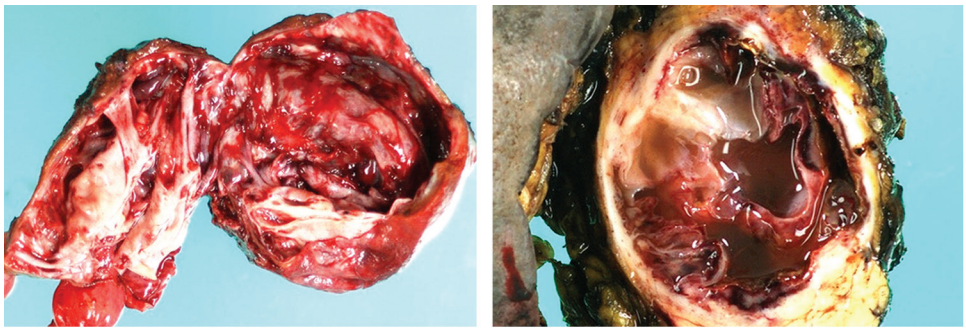
a. b.

Figure 16. Imaging findings of a cystic intraductal papillary neoplasm of the biliary tract **(a)** and the side duct type of intraductal papillary mucinous neoplasm of the pancreas **(b)**. **(a)** Axial contrast-enhanced CT image of a 59-year-old woman depicts a multilocular cystic hepatic mass (arrow) containing calcifications and enhancing septa, with a possible communication with the adjacent common bile duct containing an enhancing solid component (black arrowhead); also note the dilated bile ducts (white arrowheads) involving both lobes of the liver. The findings at histopathologic examination confirmed that this mass was a cystic intraductal papillary neoplasm of the biliary tract. **(b)** Coronal T2-weighted MR image of a 66-year-old man shows a cystic mass (arrow) with a few septa in the pancreatic tail; given the proximity of this mass to the main pancreatic duct (arrowhead), the diagnosis of side duct intraductal papillary mucinous neoplasm of the pancreas was considered at imaging. The findings at histopathologic examination confirmed this diagnosis.

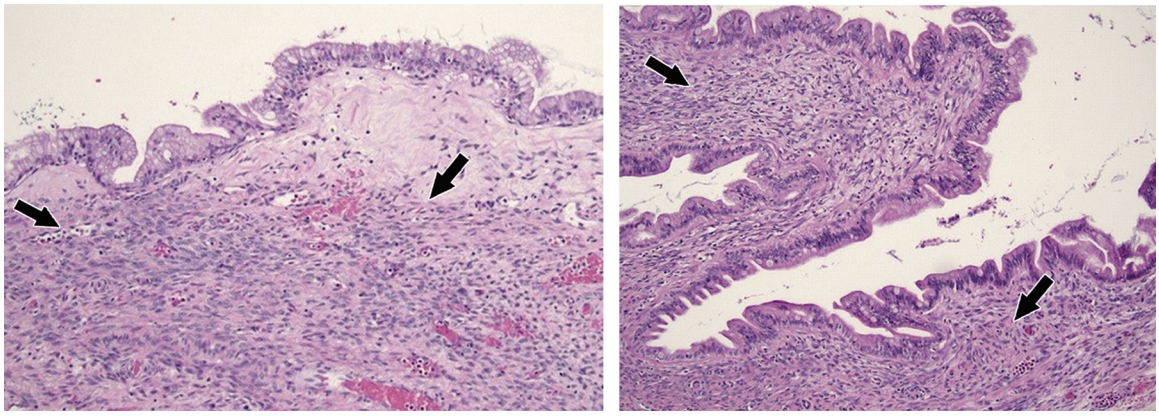
CK7, MUC1 and MUC5AC, estrogen receptor, progesterone receptor, trypsin, and amylase at variable frequencies (61).

Both tumors are typically moderate to large at cross-sectional imaging, have a well-defined fibrotic capsule and multiple internal septa, and may contain discontinuous peripheral calcifications (Fig 18) (59,62). The cyst walls are typically thick and may demonstrate delayed enhancement at contrast-enhanced imaging. The internal septa and mural nodularity may show variable enhancement after contrast material administration. At MR imaging, the cyst content is variable in signal intensity on T1-weighted MR images and is usually hyperintense on T2-weighted MR images (59,62). Typically, no communication with the adjacent ductal system can be identified at imaging.

Mucinous cystic neoplasm of the liver and pancreatic mucinous cystic neoplasm are considered low-grade malignant lesions; complete surgical excision is the treatment of choice, and, if achieved, the prognosis is excellent with both of these lesions. However, if these cysts are incompletely excised, marsupialized, or drained, the prognosis is less favorable (2,59,62).



a. c.



b. d.

Figure 17. Histopathologic findings of a hepatic mucinous cystic neoplasm in a 45-year-old woman **(a, b)** and a pancreatic mucinous cystic neoplasm in a 72-year-old woman **(c, d)**. **(a)** Photograph of a cut section of the gross specimen shows a large partially loculate smooth-walled cystic cavity filled with blood-tinged mucoid material. **(b)** High-power photomicrograph shows simple columnar epithelium with low-grade mucin-filled cells and ovarian-type stroma underneath (arrows). (H-E stain; original magnification, ×200.) **(c)** Photograph of a cut section of the gross specimen shows a large smooth-walled multilocular cystic mass containing mucoid material. **(d)** High-power photomicrograph shows single columnar epithelium of low-grade cells with scattered mucin-filled goblet cells and ovarian-type stroma underneath (arrows). (H-E stain; original magnification, ×200.)

Clinical Implications

A comprehensive and common approach is possible to study select biliary diseases and their pancreatic counterparts. Clinical and research data obtained for pancreatic diseases could be applied to the study of biliary diseases, and vice versa. Because most of the biliary and pancreatic cancers are of ductal origin, an understanding of the genetic and molecular mechanisms of ductal carcinogenesis of the pancreas and biliary tract may help to develop more-effective types of therapy and prevention. For example, on the basis of the identification of GNAS mutations in as many as 50% of intraductal papillary mucinous neoplasms of the pancreas by Furukawa et al (63), Sasaki et al (64) found frequent GNAS abnormalities in intraductal papillary neoplasms of the biliary tract, a finding that indicates a common pathogenesis. Additionally, these investigators also detected that the status of KRAS mutations was inversely correlated to MUC2 expression and that intraductal papillary neoplasms of the biliary tract with high mucin content are characterized by a perihilar location and high expression of MUC2 and MUC5A (63,64). Patients with biliary diseases may receive the benefit of novel therapeutic approaches derived from the advances in pancreatic research, and vice versa. For example, some patients with pancreatic ductal adenocarcinoma and also extrahepatic cholangiocarcinoma are shown to have a good response to chemotherapy with combination capsules of tegafur, gimeracil, and oteracil potassium (TS-1; Taiho Pharmaceutical, Tokyo, Japan) and to gemcitabine chemotherapy (65,66). Cross-sectional imaging studies play an important role in testing the efficacy of these novel drugs. Given the possibility of simultaneous occurrence of select biliary and pancreatic diseases (for example, IgG4-related sclerosing cholangitis and type 1 autoimmune pancreatitis; intraductal papillary neoplasms of the biliary tract and intraductal papillary mucinous neoplasms of the pancreas), identification of one disease will lead to the search for its counterpart (27,49).

Conclusion

Select biliary and pancreatic conditions demonstrate similarities in the gross pathologic, histopathologic, and clinical features. Many of

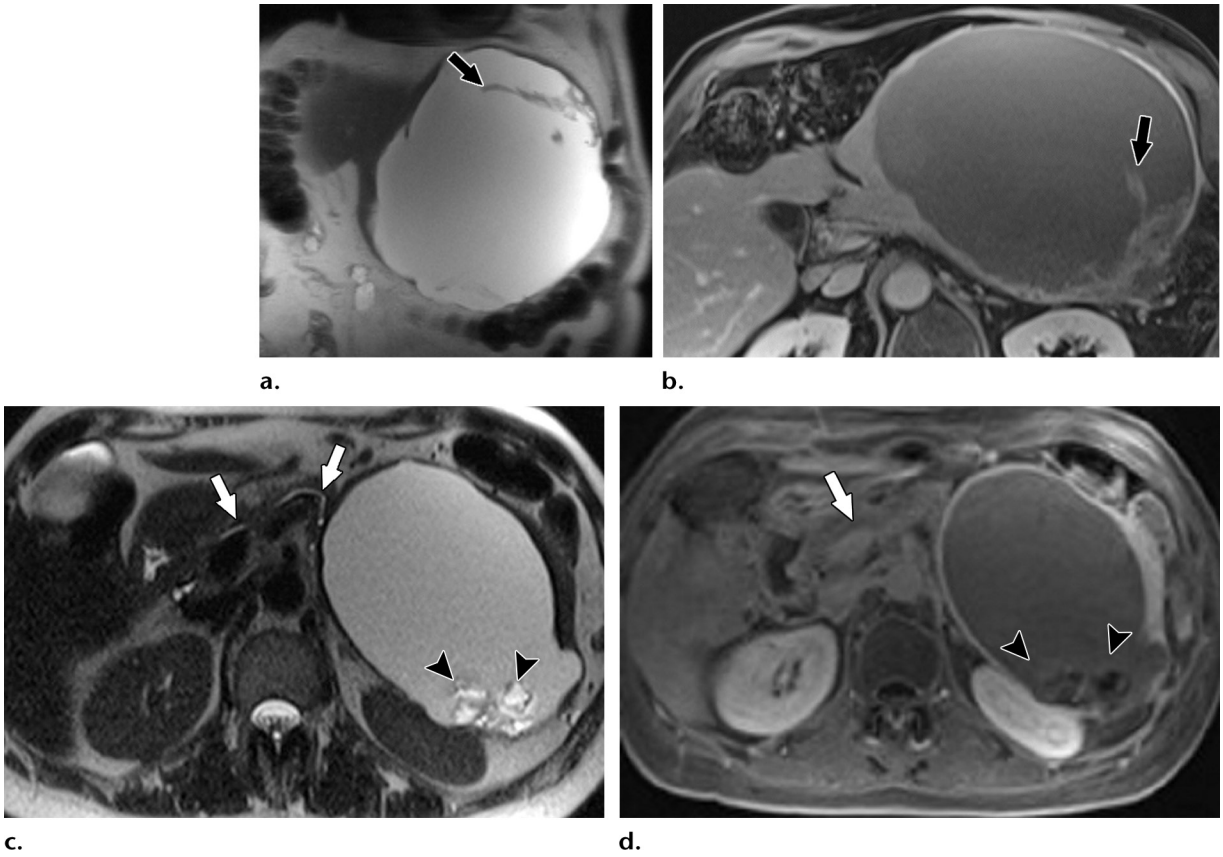


Figure 18. Imaging similarities between a hepatic mucinous cystic neoplasm in a 48-year-old woman **(a, b)** and a pancreatic mucinous cystic neoplasm in a 56-year-old woman **(c, d)**. **(a, b)** Coronal T2-weighted **(a)** and axial gadolinium-enhanced T1-weighted **(b)** MR images show a large cystic mass in the left hepatic lobe, with enhancing septa and solid components (arrow); note the absence of biliary ductal dilatation. The findings at surgical resection confirmed that this mass was a mucinous cystic neoplasm containing ovarian-type stroma. **(c, d)** Axial T2-weighted **(c)** and gadolinium-enhanced T1-weighted **(d)** MR images show a cystic mass involving the body and tail of the pancreas that contains enhancing solid components (arrowheads) in the periphery; a nondilated main pancreatic duct (arrows) is also depicted in the body and head of the pancreas. The findings at histopathologic examination confirmed that this mass was a mucinous cystic neoplasm with ovarian-type stroma.

these pathologic conditions demonstrate similar findings at cross-sectional imaging, findings that support the concept of biliary diseases with pancreatic counterparts; however, further research is warranted to establish this hypothesis. Knowledge of this unified concept may assist in understanding the pathogenesis of pancreaticobiliary diseases and in the development of novel therapeutic agents. Imaging plays a critical role in the further confirmation of this unique disease concept and in testing the efficacy of new drugs.

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