

Neoplasms of the Biliary Tract

Radiologic and Pathologic
Correlations

Jae Hoon Lim
Kee-Taek Jang
Jung Hoon Kim

Second Edition

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 Springer

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1.1 Bile Ducts

Bile is synthesized by liver cells and it is excreted into the bile canaliculi, one of the smallest bile draining structures. Individual bile canaliculi lie between walls of liver cells which form their borders [1]. These are part of a regular, fine network measuring about 0.5–1.0 μm in width connecting adjacent hepatic cells formed by grooving of the plasmalemmae of apposing hepatocytes (Fig. 1.1). They have no distinct wall of their own. Bile is excreted into these minute passageways which drain the bile centrifugally from the central vein area to the periphery of the hepatic lobules where they empty the bile into the terminal bile ductules or canals of Hering. Thus, from the bile canaliculi, bile flows towards the terminal bile ductules whereas hepatic blood flows towards the central vein.

The canal of Hering or terminal bile ductule is a short, narrow connecting channel, 10–20 μm in width, lined with low cuboidal epithelium, that transports the bile from the canaliculi to the interlobular bile ducts in the portal area (Fig. 1.2). The interlobular ductules are 30–40 μm wide, their walls lined with simple, tall cuboidal epithelial cells [1]. These ductules increase in diameter by fusing together as they proceed towards the hilum of the liver, eventually to become the right and left hepatic ducts that exit the liver at the porta hepatis. The biliary tract is lined by a single layer of cuboidal to high columnar epithelium

(cholangiocytes) depending upon the size of the bile ducts (Fig. 1.3).

The biliary tree is divided into intrahepatic and extrahepatic bile ducts. The right and left hepatic ducts and their first to third branches are collectively called the “hilar and perihilar ducts.” The first to third branch bile ducts are large intrahepatic bile ducts which are grossly visible [2] (Fig. 1.4). Bile ducts proximal to the third branches are called small intrahepatic bile ducts. These ducts consist of septal and interlobular bile ducts and are recognizable microscopically. These two bile ducts are surrounded by distinct fibrous tissue investment and accompanied by similar sized hepatic arterial branches and portal veins forming a portal triad.

The extrahepatic bile ducts consist of a proximal part, a common hepatic duct that lies between the bifurcation and the cystic duct, and a distal part or the common bile duct that lies between the cystic duct and the ampulla of Vater. Normally, the extrahepatic ducts measure 3–6 mm in diameter. The cystic duct connects the gallbladder to the extrahepatic ducts.

Around the intrahepatic large bile duct and extrahepatic duct are innumerable, tiny peribiliary glands [3] (Fig. 1.4). Embryologically, these glands also derive from the ductal plate which gives rise to the normal biliary tree [4]. The peribiliary glands can be divided into intramural and extramural types (Fig. 1.5). The former are scattered within the bile duct walls and are

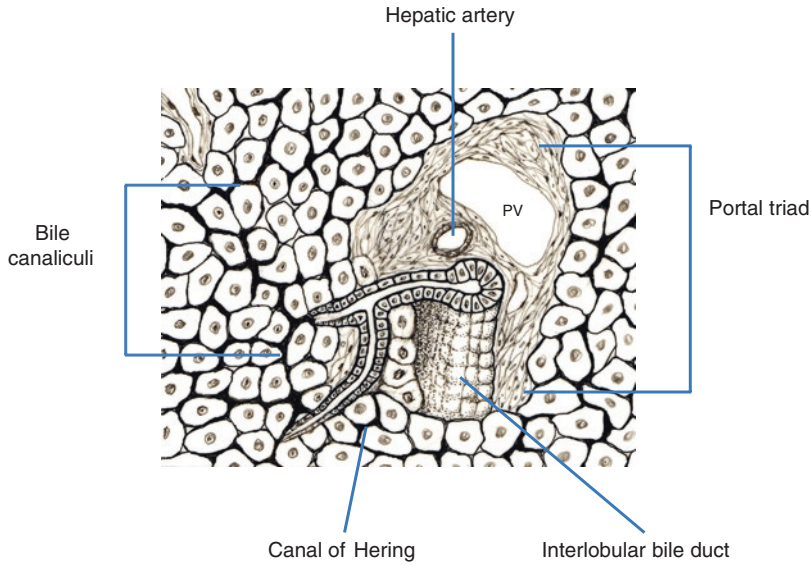
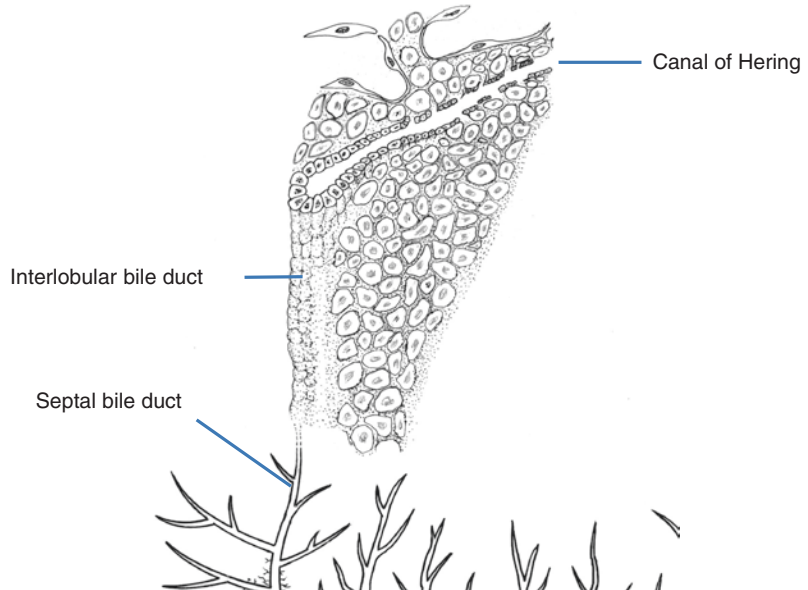


Fig. 1.1 Schematic drawing of bile production and drain. Bile is produced by hepatocytes and drain into the bile canaliculi, canals of Hering, and then interlobular bile ductules. Bile canaliculi are formed by the grooving of plasmalemmae of apposing hepatocytes. Canals of Hering

are short channels lined with low cuboidal epithelium and connect bile canaliculi and interlobular bile ductules. Interlobular bile ductules are lined with tall cuboidal epithelium and lie in the portal space

Fig. 1.2 Schematic drawing of anatomy of canals of Hering, interlobular bile ducts, and septal bile ducts. These bile ducts are not grossly visible and recognized microscopically. The interlobular bile ducts and septal bile ducts are in the portal triad and accompanied by portal veins and hepatic arteries. (Modified from Ref. [1])



simple tubular glands with mucous epithelium. The latter are located in the periductal connective tissue and are branched tubuloalveolar sero-mucous glands. Observations of serial sections revealed that the extramural glands drain into

the large bile duct lumina via their own conduits while the intramural glands drain directly into the bile duct lumen.

Histologically, bile duct wall is composed of epithelium with scanty lamina propria and fibro-

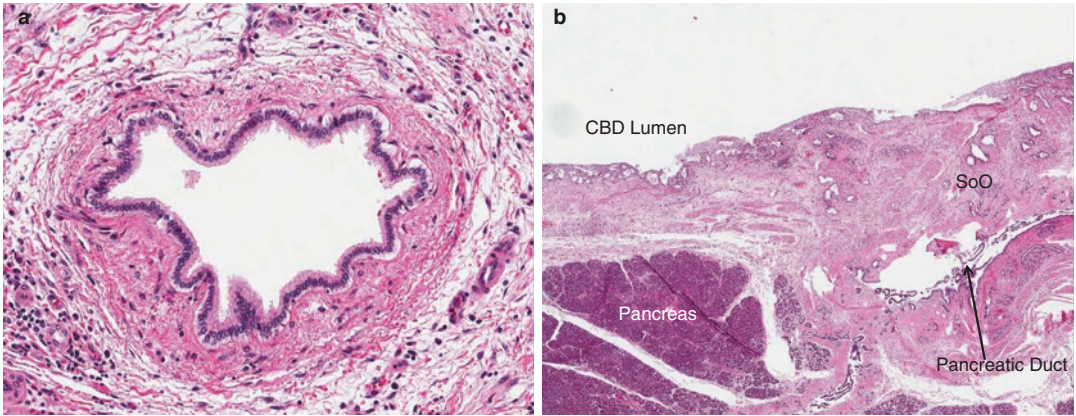


Fig. 1.3 Normal bile duct. (a) Microphotograph of intrahepatic duct shows portal space and bile duct wall comprising single layer of cuboidal to columnar epithelium and surrounding fibroareolar tissue (H&E stain, $\times 100$). (b) The extrahepatic bile ducts consist of mucosa and

fibromuscular layer. The distal portion of extrahepatic bile duct has relatively distinct muscle fibers, and these muscle fibers are merged into muscle fibers of sphincter of Oddi (SoO) and duodenum (H&E stain, $\times 10$)

Fig. 1.4 Schematic drawing of intra- and extrahepatic bile ducts. The right and left hepatic ducts and their first to third branches are collectively called large bile ducts and they are grossly visible. Around these bile ducts are innumerable peribiliary glands

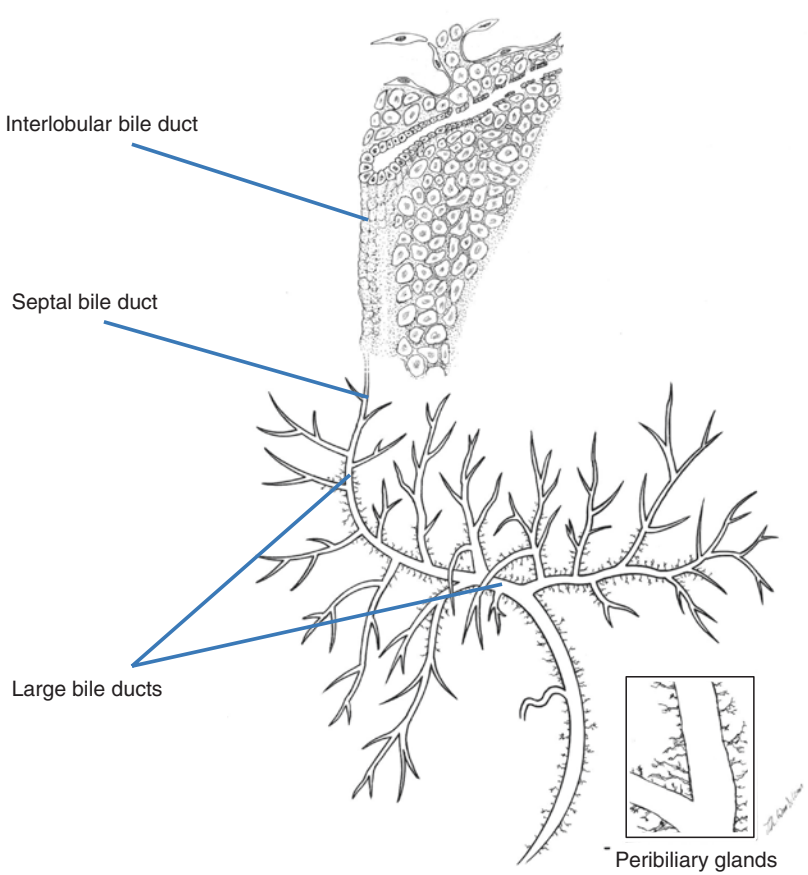
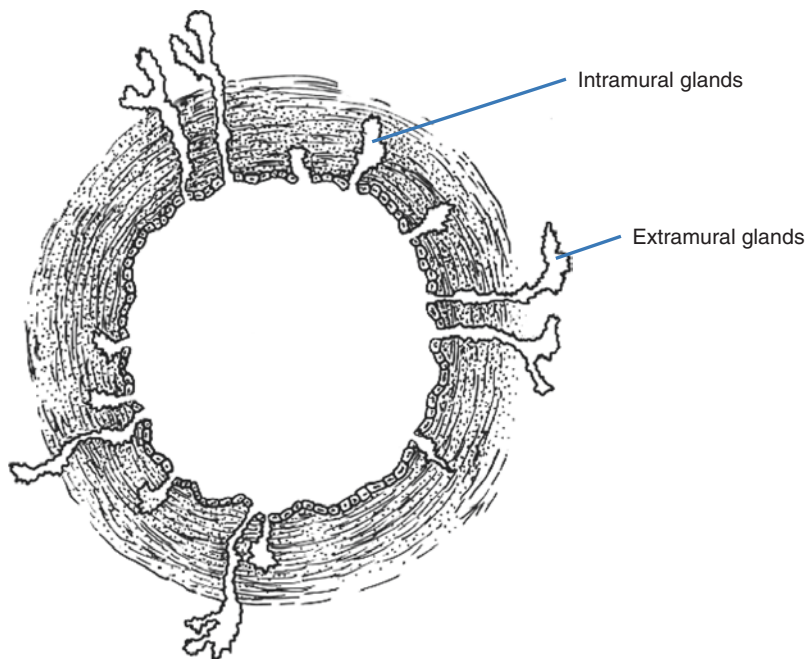


Fig. 1.5 Schematic drawing of peribiliary glands. There are two types of peribiliary glands, namely intramural and extramural types. Intramural peribiliary glands are simple tubular mucous glands scattered within the bile duct walls, and extramural glands are branched tubuloalveolar seromucous glands, located in the periductal tissue



muscular layer with scattered peribiliary glands. Fibromuscular layer of bile duct wall is composed of fibrous tissue and intermixed smooth muscle fibers beneath the epithelium. In the common bile duct are oblique and longitudinal layers of muscles [1]. As the duct approaches the duodenum, these muscle layers become more distinct gaining more circular fibers. At the ampullary portion, these muscles form a potent sphincter (sphincter of Oddi) (Fig. 1.3), which regulates the emptying of bile into the duodenum. The adventitia of the extrahepatic ducts is largely composed of loose areolar tissue and collagen fibers. There is no serosal membrane outside the extrahepatic ducts.

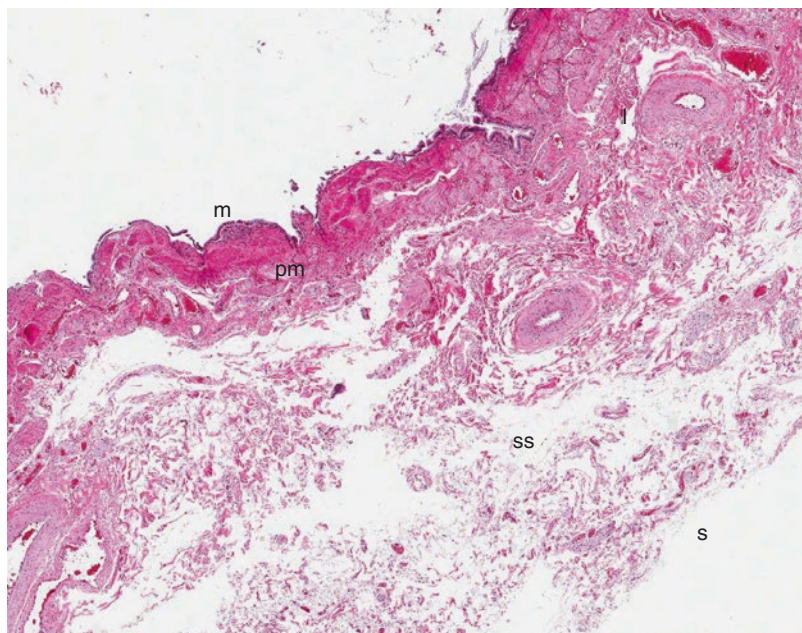
1.2 Gallbladder

The gallbladder is a pear-shaped, hollow bag; its wall consists of the mucosa, muscle, and serosal covering. It arises from an outpocketing of the common hepatic duct. The gallbladder is divided by a large blind-ending, rounded fundus, a cylindrical main portion which forms the body, a continuously narrow neck, and a cystic duct which connects the gallbladder and common hepatic

ducts. Usually, it measures about 50–90 ml in volume, 7–10 cm in length, and about 2–3 cm in width. It is attached to the undersurface of the right and left hepatic lobe. When a kinking or folding of a part of the fundus occurs, it is anatomically separated from the rest and is called a Phrygian cap.

The gallbladder wall consists of a mucosal layer thrown in folds and lined by tall columnar epithelium, a muscular layer, a subserous layer, and a serosal layer (Fig. 1.6). Unlike the gastrointestinal tract, there is no muscularis mucosae and submucosal layer in the gallbladder wall. Irregular, velvety or villous, redundant mucosal folds or rugae, subdivided into minute folds, are easily seen in a contracted state yet disappear on extreme distension. Under the columnar epithelium, there is a thick lamina propria consisting of richly vascularized loose areolar supporting tissue. The lamina propria of the neck and cystic duct contains numerous mucous glands. The mucosa and muscular layers of the cystic duct are continuous with those of the extrahepatic duct and thus pathologic process of the gallbladder may extend to the extrahepatic ducts, and vice versa.

Fig. 1.6 Gallbladder wall. Microphotograph shows gallbladder wall consisting of mucosa (m) lined by columnar epithelial layer, lamina propria (l), proper muscle layer (pm), subserosal space (ss), and serosal membrane (s). (H&E stain, $\times 40$)



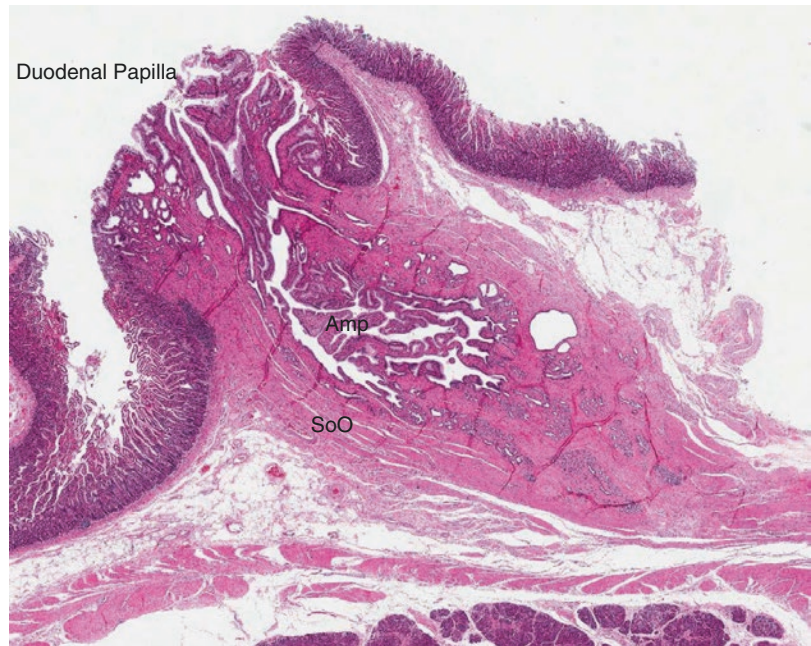
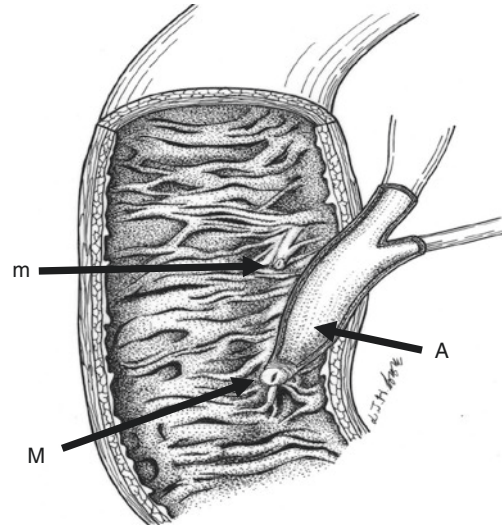
1.3 Ampulla of Vater and Duodenal Papilla

The distal common bile duct and main pancreatic duct come into contact at the medial side of the descending part of the duodenum. The two ducts separately pass through the wall of the duodenum obliquely, and there the two ducts usually unite to form a short, dilated tube which is named hepatopancreatic ampulla (or ampulla of Vater) (Figs. 1.7 and 1.8). The narrow, distal end of this ampulla opens on the summit of a nipple-like projection, major duodenal papilla, which is situated within the descending part of the duodenum at the junction of its medial and posterior walls. Therefore, ampulla of Vater refers to the inside of the hepatopancreatic duct whereas duodenal papilla refers to a nipple-like projection into the duodenum, outside the ampulla of Vater (Figs. 1.9 and 1.10). The length of normal papilla is a few millimeters. The ampulla

of Vater is lined by simple columnar epithelium like the common bile duct, whereas the duodenal papilla is lined by intestinal mucosa similar to colonic epithelium. The accessory pancreatic duct opens about 2 cm proximal to the major papilla, on a small rounded minor duodenal papilla (Fig. 1.7).

The sphincter of Oddi refers to the circular muscle complex around the ampulla of Vater and the common bile duct and pancreatic duct just before union. Therefore, the sphincter of Oddi consists of sphincter ampullae, sphincter choledochus, and sphincter pancreaticus (Fig. 1.11). Sphincter ampullae, variably developed, are an annular muscle extending from the junction of the ducts to the tip of major papilla. Because of the contraction of the sphincter of Oddi, the ampullary segment is not commonly visualized on ERCP (Fig. 1.12). It is the muscle of the common channel and is responsible for the potential reflux of pancreatic juice into the bile duct.

Fig. 1.7 (a) Schematic drawing of the ampulla of Vater and duodenal papilla. A = ampulla of Vater, M = major papilla, m = minor papilla. (b) Microphotograph of resected duodenal papilla shows low magnification view of ampulla of Vater, consisting of sphincter of Oddi (SoO), ampulla (Amp), and duodenal papilla. (H&E stain, $\times 10$)



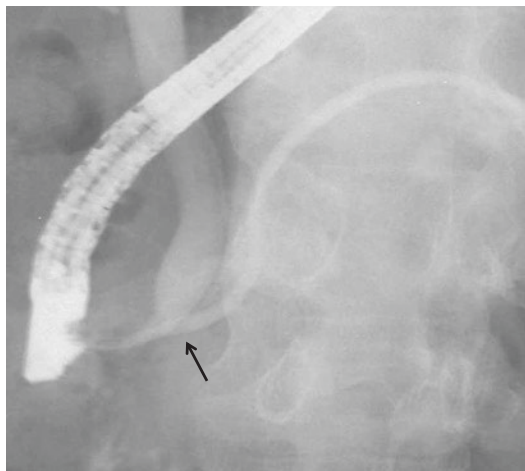


Fig. 1.8 Ampulla of Vater. ERCP shows a union of the common bile duct and main pancreatic duct to form ampullary segment (arrow) draining into the duodenum

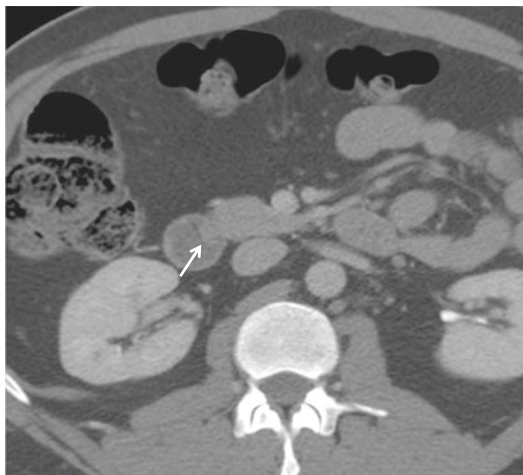


Fig. 1.10 Normal duodenal papilla. CT shows a small nodular projection of the duodenal papilla into the lumen (arrow), measuring 7 mm in diameter

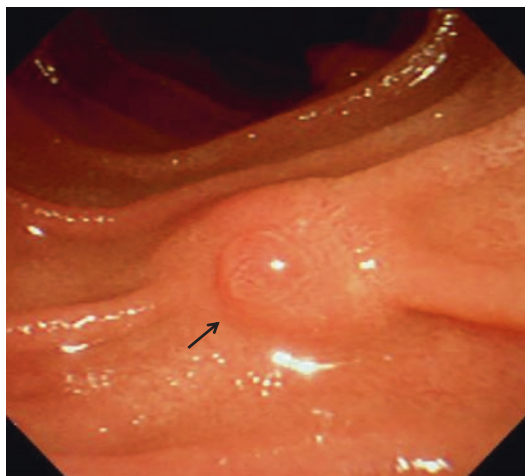


Fig. 1.9 Duodenal papilla. Duodenal endoscopy shows normal major papilla (arrow)

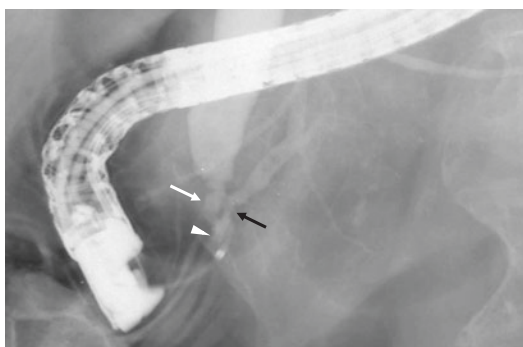


Fig. 1.11 Sphincter of Oddi. ERCP shows contraction of the sphincter choledochus (white arrow), sphincter pancreaticus (black arrow), and sphincter ampulla (arrowhead)

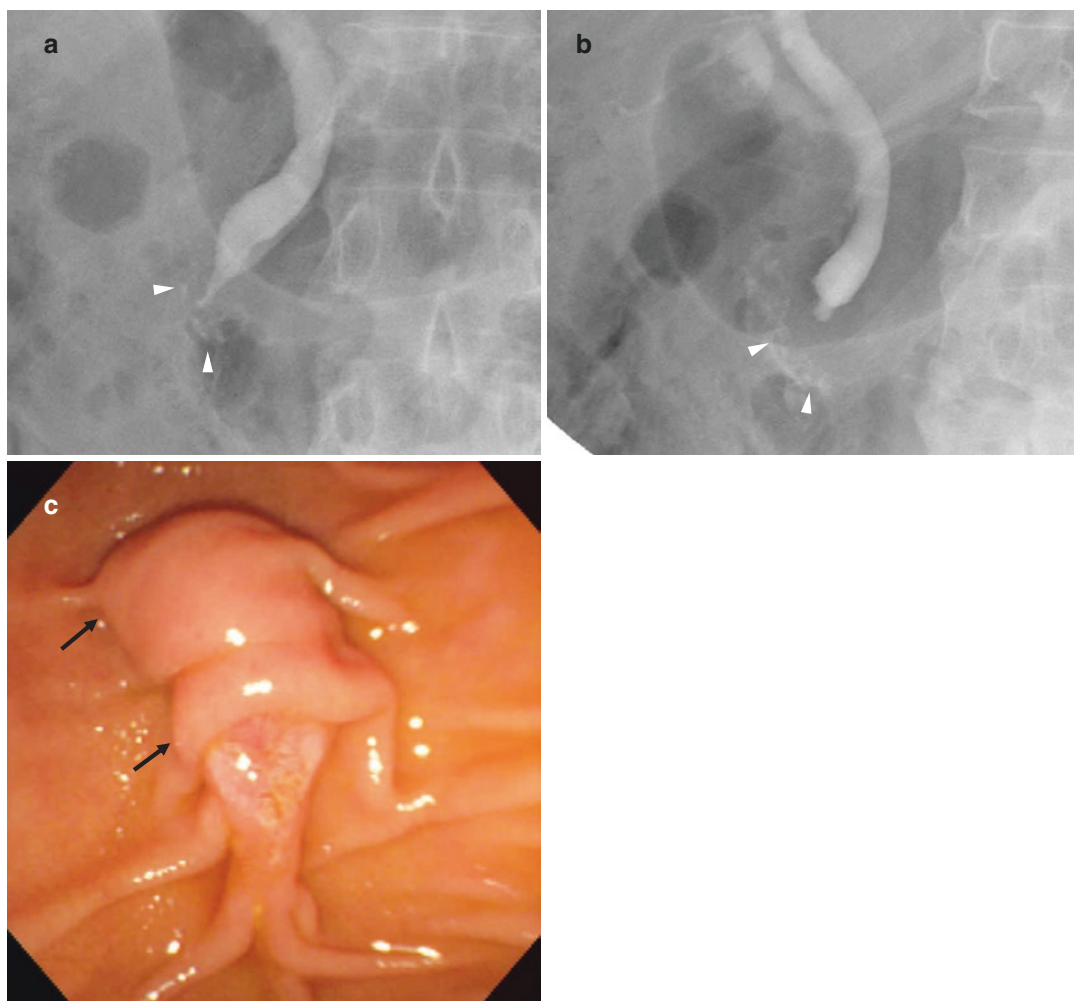


Fig. 1.12 Normal sphincteric muscle contraction. (a) ERCP shows tapering of the ampullary segment (arrowhead). (b) ERCP several second later shows nonvisualization of the ampullary segment owing to contraction of the

sphincter of Oddi. Arrowheads point to duodenal papilla. (c) Duodenal endoscopy shows prominent major papilla (arrows) due to hypertrophic sphincter muscles

References

1. Telford IR, Bridgman CH. Introduction to functional histology. New York: Harper & Row; 1990.
2. Nakanuma Y, Sato Y, Harada K, Sasaki M, Xu J, Ikeda H. Pathological classification of intrahepatic cholangiocarcinoma based on a new concept. *World J Hepatol.* 2010;2:419–27.
3. Nakanuma Y. A novel approach to biliary tract pathology based on similarities to pancreatic counterparts: is the biliary tract an incomplete pancreas? *Pathol Int.* 2010;60:419–29.
4. Terada T, Nakanuma Y. Development of human intrahepatic peribiliary glands. Histological, keratin immunohistochemical, and mucus histochemical analyses. *Lab Investig.* 1993;68:261–9.

2.1 Simple (Bile Duct) Cyst

Cysts arising in the liver are usually called hepatic cysts. The size of these cysts is widely variable, from barely visible to measuring nearly 20 cm in diameter. The number in which these cysts are found is also widely variable, from single cysts to groups of cysts that are too numerous to count. Hepatic cysts are quite common in many adults; in fact, the hepatic cyst is the most common benign lesion in the liver.

Although called hepatic cysts, these cysts actually arise from the bile ducts. Microscopically, hepatic cysts are characterized by a cuboidal or simple columnar epithelial lining containing serous fluid and various epithelial products (Fig. 2.1). The cyst wall is composed of thin fibrous tissue. Since most cysts occur in adults, their incidence increasing with age, these cysts are presumed to be acquired. They do not communicate with the bile ducts. It is thought that a cyst represents the retention of fluid in the bile duct derivation [1, 2]. The lining cells or any part of the cysts does not contain hepatocytes or hepatocyte derivatives (Fig. 2.2). Accordingly calling cysts in the liver biliary cysts is more accurate than referring to them as hepatic cysts.

The vast majority of cysts are stationary but some cysts grow (Fig. 2.3). When a cyst becomes excessively large, compressive symptoms may occur on rare occasions. They may induce bile duct compression and obstructive jaundice.

Sometimes, cysts may shrink (Fig. 2.4), disappear, or rupture due to trauma. They rarely rupture spontaneously (Fig. 2.5).

On ultrasound or CT, simple cysts appear smooth, round, or oval well-defined, echo free, or homogeneously hypodense like water-attenuation globes (Figs. 2.1, 2.3, and 2.5). They are depicted as low signal intensity globes on T1-weighted images and very high signal intensity globes on T2-weighted images. The walls are not visualized when the cysts are surrounded by liver parenchyma. When cysts bulge out of the hepatic margin, the wall is barely visible or not visible at all (Fig. 2.3). When inflammation or hemorrhage occurs, there may be echogenic debris on ultrasound, CT attenuation value increases, and MR signal intensity undergoes a variety of changes depending upon the content of the cyst or age of hemorrhage.

Some simple cysts may have one or few internal septa (Fig. 2.6). When two or several cysts arise in the same area, those cysts abut each other and the intervening fibrous or compressed liver tissue looks like septa' (Fig. 2.7). In these cases, differential diagnosis from mucinous cystic neoplasm may be difficult. In a mucinous cystic neoplasm, the cyst is a multiloculated single cyst possessing one large round boundary exhibiting a smooth margin. On the other hand, in clustered multiple simple cysts, the boundary of the cysts is lobulated or wavy because these cysts arise individually and cluster in small regions (Fig. 2.7).

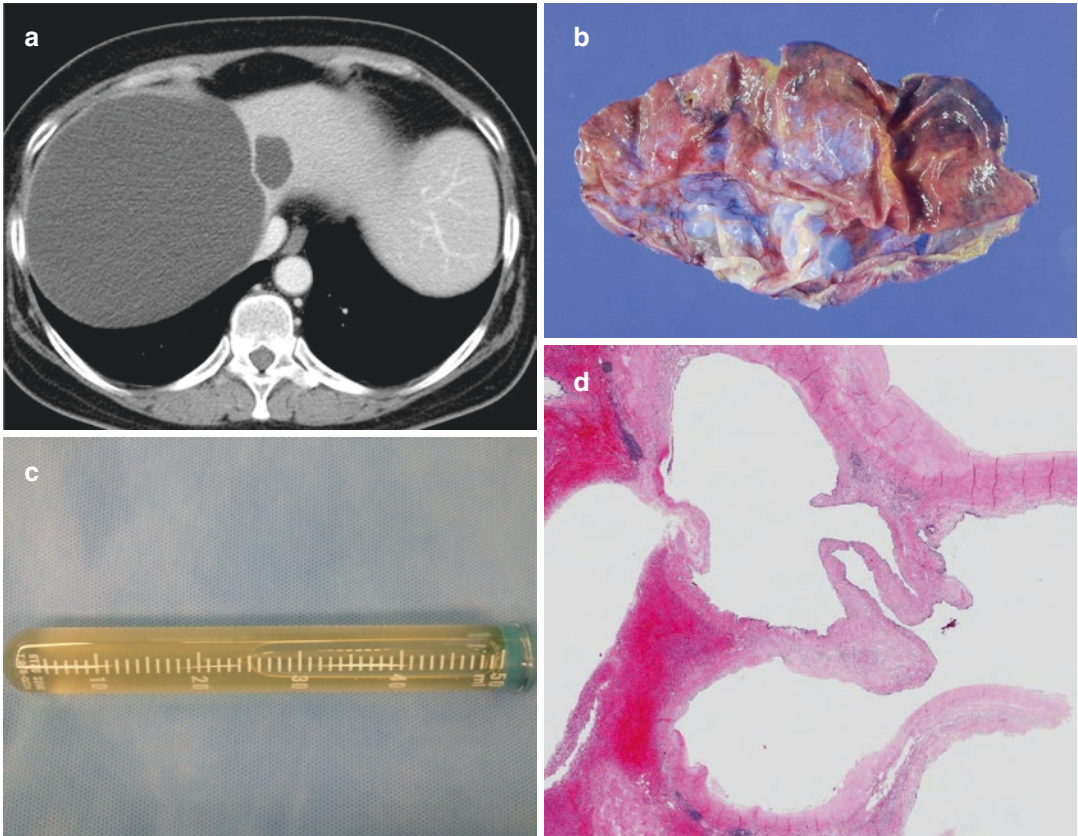


Fig. 2.1 Simple cyst. (a) Contrast-enhanced CT images show two cysts, measuring 15 and 3 cm, occupying the major part of the right hepatic lobe. The cyst wall is imperceptible because the thin cyst wall blends with the surrounding liver parenchyma and diaphragm. (b)

Resected specimen shows a thin membrane-like cyst wall. (c) Clear, yellowish serous fluid evacuated from the cyst. (d) Photomicrograph shows corrugated fibrous capsule (H&E stain, ×10)

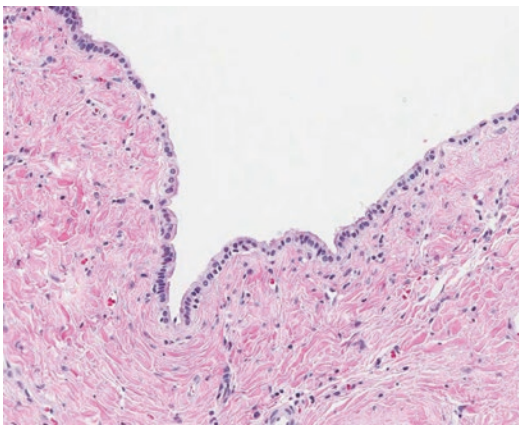


Fig. 2.2 Microphotograph of the cyst wall. The luminal side is lined by a single layer of cuboidal-to-columnar epithelial cells with subepithelial fibrous wall. There is no hepatocyte or hepatocytic derivative (H&E stain, ×200)

2.2 Ciliated Hepatic Foregut Cyst

Ciliated hepatic foregut cysts derive from the remnants of the embryonal foregut that are embedded inside the hepatic bud during embryogenesis. The cyst wall is lined with ciliated pseudostratified columnar epithelial cells (Fig. 2.8). It is usually found incidentally during cross-sectional imaging. Squamous cell carcinomas may develop from these cysts [3].

On imaging, ciliated hepatic foregut cysts present with a small solitary unilocular cyst in the liver, measuring 3 cm or smaller, these cysts being filled with viscous mucinous fluid [4]. Typically, these cysts are located superficially in the medial segment of the left hepatic lobe. The

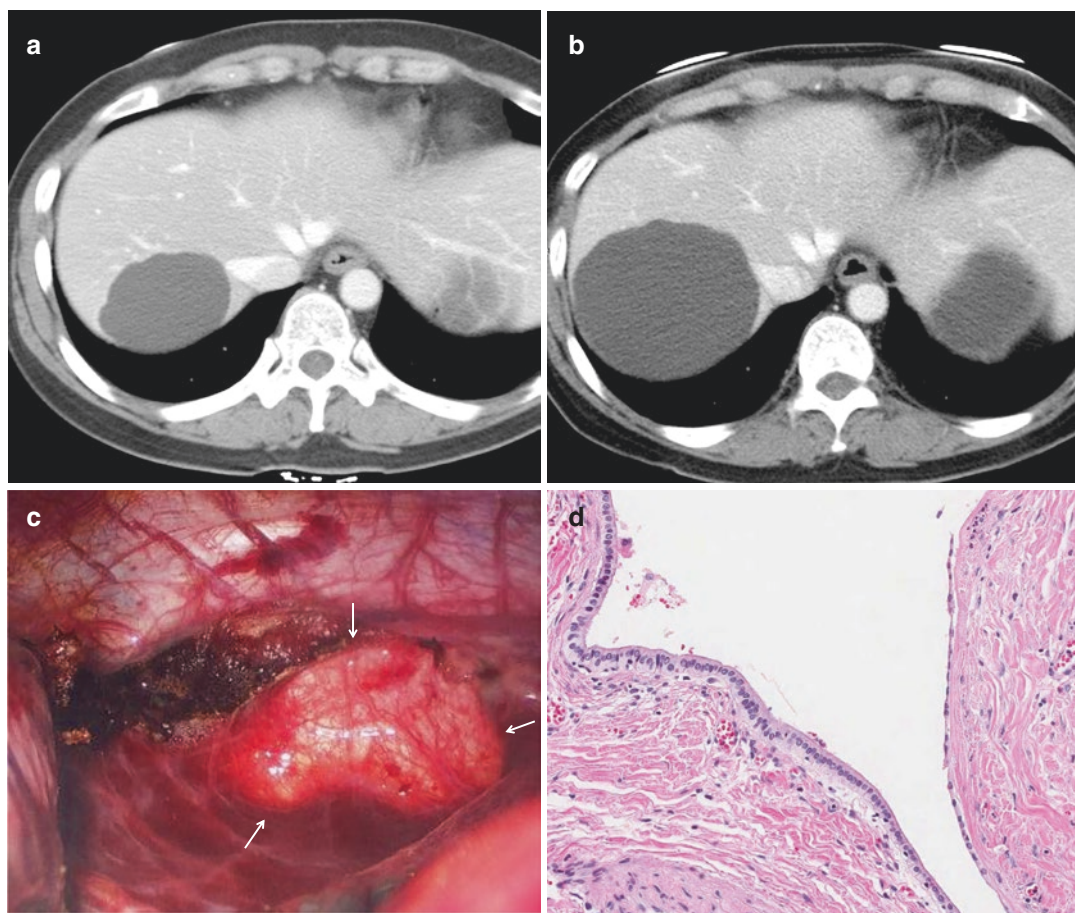


Fig. 2.3 Simple cyst, growing. (a) CT image shows a cyst measuring 6 cm in diameter. Cyst wall is imperceptible. (b) CT image 5 years later shows the same cyst measuring 10 cm in diameter. (c) Photograph at operation

shows a bulging cyst (arrows) from the liver surface. (d) Microphotograph shows the cyst wall, which is lined by a single layer of tall columnar epithelial cells (left) and flattened epithelial cells (right) (H&E stain, $\times 200$)

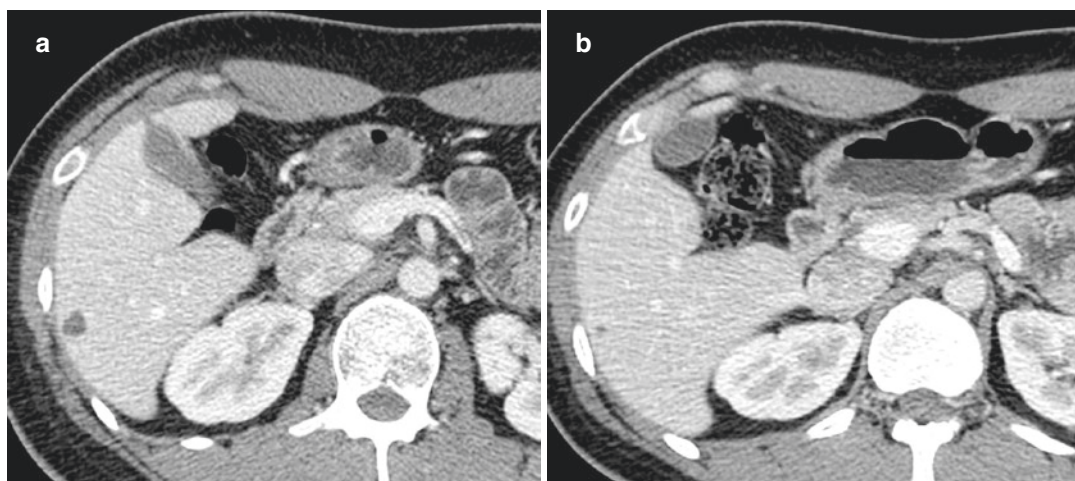


Fig. 2.4 Simple cyst, shrinking. (a) CT image shows a cyst measuring 10 mm in diameter. (b) CT image 10 months later shows the cyst measuring 2 mm in diameter

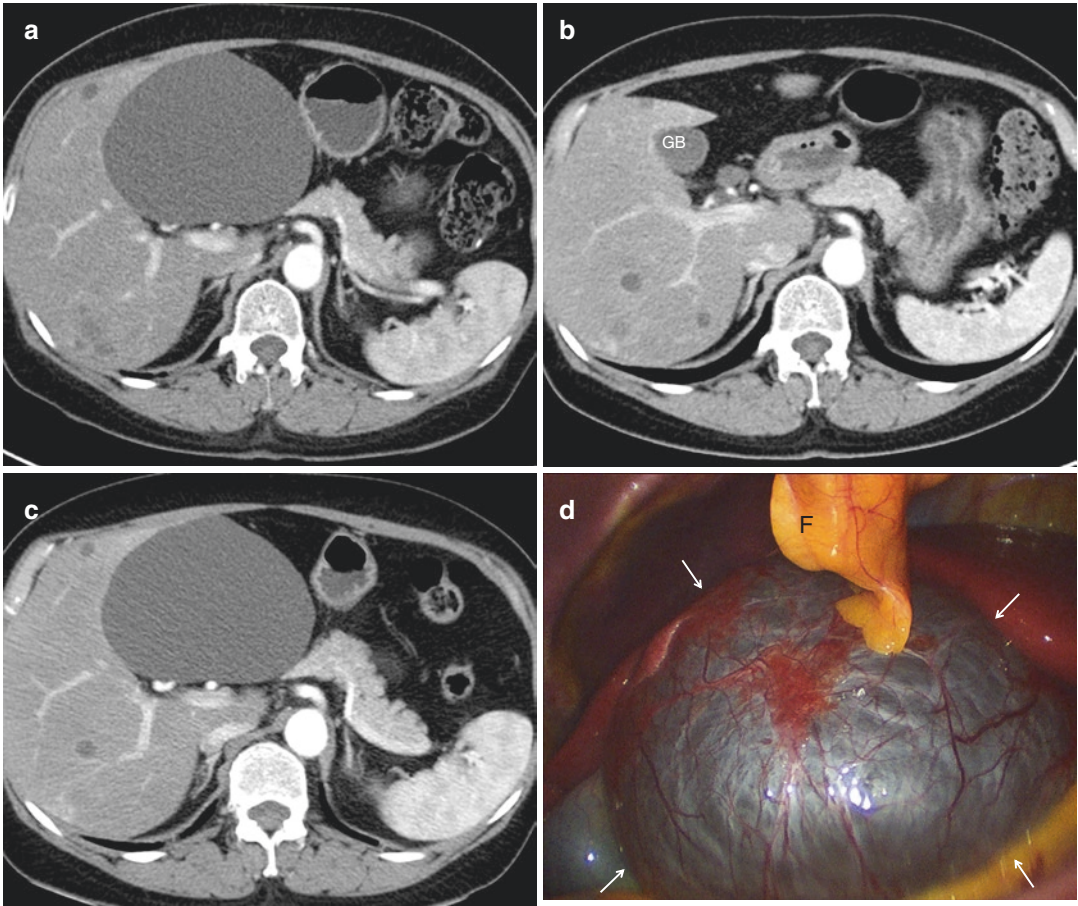


Fig. 2.5 Simple cyst with rupture and regrowth. (a) Contrast-enhanced CT image shows a cyst, measuring 12 cm in diameter. Cyst wall is imperceptible. (b) CT image 6 months later shows no cyst indicating rupture and

disappearance of the cyst. *GB* gallbladder. (c) CT image 18 month later shows regrowth of the cyst, measuring 12 cm in diameter. (d) Photograph at operative field shows a cyst bulging out the liver (arrows)

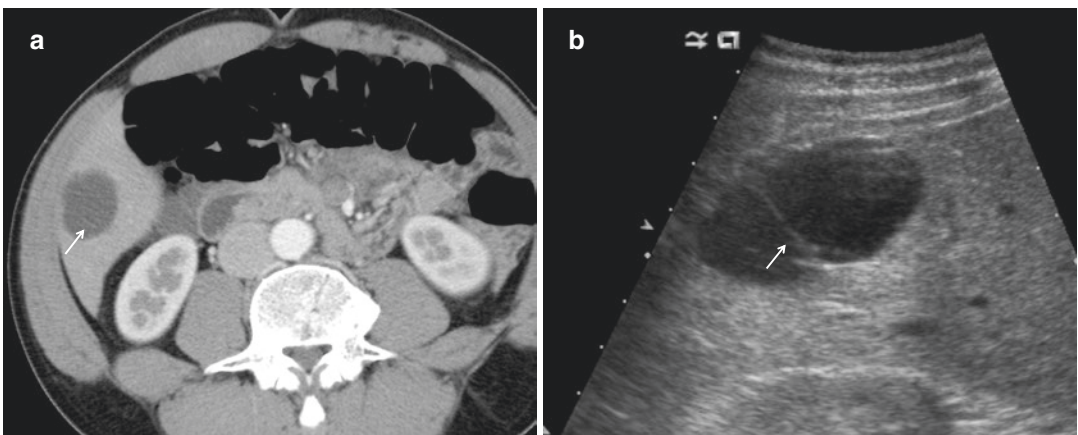


Fig. 2.6 Septated simple cyst. (a) Contrast-enhanced CT image shows an oval cyst containing a barely visible septa (arrow). (b) Ultrasonogram shows an oval cyst containing a thin septa (arrow)