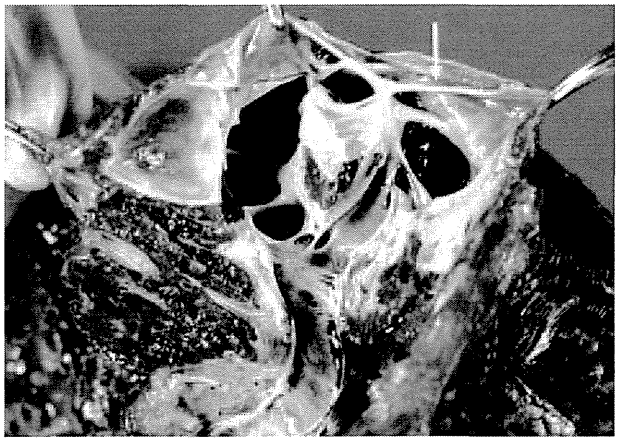

FIGURE 111-11 Gross pathology sections of the liver in Caroli disease show multiple saccular dilations of the intrahepatic bile ducts and black-pigmented calcium bilirubinate stones. Septum-like fibrovascular bundles *(arrow)* are seen on the walls of the cut sacculi.

magnetic resonance imaging, and CT have been shown to be useful in detecting saccular dilation of the intrahepatic bile ducts. The sacculi may vary greatly in size and distribution within the liver.[51] CT scans of the liver show tiny dots with strong contrast enhancement within the dilated intrahepatic bile ducts or the "central dot sign," which corresponds to intraluminal portal radicles surrounded by the dilated intrahepatic bile ducts (Figure 111-11).[51,55]

The long-term prognosis for patients with Caroli disease is quite poor, with a marked predisposition to septicemia, liver abscess, resultant hepatic failure, portal hypertension, or cholangiocarcinoma.[53] Cholangiocarcinoma has been reported in about 7% of patients.[53,54] The therapeutic management of Caroli disease is difficult, whether using conservative medical management or surgical interventions. Liver transplantation should be considered if the patient's condition deteriorates.[56,57]

REFERENCES

1. Alonso-Lej F, Rever WB, Pessagno DJ: Congenital choledochal cysts, with a report of 2, and an analysis of 94, cases. *Int Abst Surg* 108:1, 1959.
2. Todani T, Wastanabe Y, Narusue M, et al: Congenital bile duct cysts: Classifications, operative procedures, and review of 37 cases including cancer arising from choledochal cyst. *Am J Surg* 134:263, 1977.
3. Todani T: Congenital choledochal dilatation: Classification, clinical features, and long-term results. *J Hepatobiliary Pancreat Surg* 4:276, 1997.
4. Stringer MD: Choledochal cysts. In Howard ED, Stringer MD, Colombani PM, editors: *Surgery of the liver, bile ducts and pancreas in children*, London, 2002, Arnold, p 149.
5. Douglas AH: Case of dilatation of the common bile duct. *Month J Med Sci* 14:97, 1852.
6. Benjamin IS: Biliary cystic disease: The risk of cancer. *J Hepatobiliary Pancreat Surg* 10:335, 2003.
7. Yamaguchi M: Congenital choledochal cyst: Analysis of 1433 patients in the Japanese literature. *Am J Surg* 140:653, 1980.
8. Nagorney DM: Choledochal cysts in adults. In Blumgart LH, Fong Y, editors: *Surgery of the liver and biliary tract*, ed 3, London, 2000, Saunders, p 1229.
9. Lugo-Vicente HL: Prenatally diagnosed choledochal cysts: Obstruction or early surgery? *J Pediatr Surg* 30:1288, 1995.
10. Kozumi I, Kodama T: A case report and etiology of choledochal cystic dilatation (in Japanesese). *J Tokyo Med Assoc* 30:1413, 1916.
11. Babbitt DP: Congenital choledochal cysts: New etiological concept based on anomalous relationships of common bile duct and pancreatic bulb. *Ann Radiol* 12:231, 1969.
12. Komi N, Takehara H, Kunitomi K, et al: Does the type of anomalous arrangement of pancreaticobiliary ducts influence the surgery and prognosis of choledochal cyst? *J Pediatr Surg* 27:728, 1992.
13. Matsumoto Y, Fujii H, Itakura J, et al: Pancreaticobiliary maljunction: Pathophysiological and clinical aspects and the impact on biliary carcinogenesis. *Arch Surg* 388:122, 2003.
14. Ando H, Kaneko K, Ito F, et al: Embryogenesis of pancreaticobiliary maljunction inferred from development of duodenal atresia. *J Hepatobiliary Pancreat Surg* 6:50, 1999.
15. The Japanese study group on pancreaticobiliary maljunction (JSPBM): Diagnostic criteria of pancreaticobiliary maljunction. *J Hepatobiliary Pancreat Surg* 1:219, 1994.
16. Kattepura S, Nanjegowda NB, Babu MK, et al: Macroscopic pancreatic heterotopia on a congenital biliary dilatation. *Pediatr Surg Int* 26:847, 2010.
17. Kaneko K, Ando H, Ito T, et al: Protein plugs cause symptoms in patients with choledochal cysts. *Am J Gastroenterol* 92:1018, 1997.
18. Kim MJ, Han SJ, Yoon CS, et al: Using MR cholangiopancreatography to reveal anomalous pancreaticobiliary ductal union in infants and children with choledochal cysts. *Am J Roentgenol* 179:209, 2002.
19. Lam WW, Lam TP, Saing H, et al: MR cholangiography and CT cholangiography of pediatric patients with choledochal cysts. *Am J Roentgenol* 173:401, 1999.
20. Aoki H: Pathology of the pancreaticobiliary maljunction. In Aoki H, editor: *Questionnaire survey for bile duct cancer complicated with pancreaticobiliary maljunction*, Toyoake, 1985, The Japanese Study Group on Pancreaticobiliary Maljunction (JSPBM), p 34.
21. Lee MJ, Kim MJ, Yoon CS: MR cholangiopancreatography findings in children with spontaneous bile duct perforation. *Pediatr Radiol* 40:687, 2010.
22. Ando H, Ito T, Watanabe Y, et al: Spontaneous perforation of choledochal cyst. *J Am Coll Surg* 181:125, 1995.
23. Irwin ST, Morison JE: Congenital cyst of the common bile duct containing stones and undergoing cancerous change. *Br J Surg* 32:319, 1944.
24. Watanabe Y, Toki A, Todani T: Bile duct cancer developed after cyst excision for choledochal cyst. *J Hepatobiliary Pancreat Surg* 6:207, 1999.
25. Hasumi A, Matsui H, Sugioka A, et al: Precancerous conditions of biliary tract cancer in patients with pancreaticobiliary maljunction: Reappraisal of nationwide survey in Japan. *J Hepatobiliary Pancreat Surg* 7:551, 2000.
26. Voyles CR, Smadja C, Shands WC, et al: Carcinoma in choledochal cysts. Age-related incidence. *Arch Surg* 118:986, 1983.
27. Tanaka S, Kubota M, Yagi M, et al: An 11-year-old male patient demonstrating cholangiocarcinoma associated with congenital biliary dilatation. *J Pediatr Surg* 41:e15, 2006.
28. Kato T, Hebiguchi T, Matsuda K, et al: Action of pancreatic juice on the bile duct: Pathogenesis of congenital choledochal cyst. *J Pediatr Surg* 16:146, 1981.
29. Todani T, Watanabe Y, Toki A, et al: Carcinoma related to choledochal cysts with internal drainage operations. *Surg Gynec Obstet* 164:51, 1987.
30. Tocchi A, Mazzoni G, Liotta G, et al: Late development of bile duct cancer in patients who had biliary-enteric drainage for benign diseases: A follow-up study of more than 1,000 patients. *Ann Surg* 234:210, 2001.
31. Ando H, Kaneko K, Ito T, et al: Complete excision of the intrahepatic portion of choledochal cysts. *J Am Coll Surg* 183:317, 1996.
32. Ando H, Kaneko K, Ito F, et al: Surgical removal of protein plugs complicating choledochal cysts: Primary repair after adequate opening of the pancreatic duct. *J Pediatr Surg* 33:1265, 1998.
33. Chiba K, Kamisawa T, Egawa N: Relapsing acute pancreatitis caused by protein plugs in a remnant choledochal cyst. *J Hepatobiliary Pancreat Sci* 17:729, 2010.
34. Ando H, Ito T, Kaneko K, et al: Congenital stenosis of the intrahepatic bile duct associated with choledochal cyst. *J Am Coll Surg* 181:426, 1995.
35. Todani T, Watanabe Y, Toki A, et al: Reoperation for congenital choledochal cyst. *Ann Surg* 207:142, 1988.
36. Ando H, Kaneko K, Ito F, et al: Operative treatment of congenital stenoses of the intrahepatic bile ducts in patients with choledochal cyst. *Am J Surg* 173:491, 1997.

37. Saing H, Han H, Chan KL, et al: Early and late results of excision of choledochal cysts. *J Pediatr Surg* 32:1563, 1997.
38. Uno K, Tsuchida Y, Kawarasaki H, et al: Development of intrahepatic cholelithiasis long after primary excision of choledochal cyst. *J Am Coll Surg* 183:583, 1996.
39. Chijiiwa K, Tanaka M: Late complications after excisional operation in patients with choledochal cyst. *J Am Coll Surg* 179:139, 1994.
40. Ishibashi T, Kasahara K, Yasuda Y, et al: Malignant change in the biliary tract after excision of choledochal cyst. *Br J Surg* 84:1687, 1997.
41. Goto N, Yasuda I, Uematsu, T, et al: Intrahepatic cholangiocarcinoma arising 10 years after the excision of congenital extrahepatic biliary dilatation. *J Gastroenterol* 36:856, 2001.
42. Hewitt PM, Kringe JEJ, Bomman PC, et al: Choledochal cysts in adults. *Br J Surg* 82:382, 1995.
43. Wheeler WIC: An unusual case of obstruction to the common bileduct (choledochocele?) *Br J Surg* 27:446, 1940.
44. Scholz FJ, Carrera GF, Larsen CR: The choledochocele: Correlation of radiological, clinical and pathological findings. *Radiology* 118:25, 1976.
45. Masetti R, Antinori A, Coppola R, et al: Choledochocele: Changing trends in diagnosis and management. *Surg Today* 26:281, 1996.
46. Schimpl G, Sauer H, Goriupp U, et al: Choledochocele: Importance of histological evaluation. *J Pediatr Surg* 28:1562, 1993.
47. Ladas SD, Katsogridakis I, Tassios P, et al: Choledochocele, an overlooked diagnosis: Report of 15 cases and review of 56 published reports from 1984 to 1992. *Endoscopy* 27:233, 1995.
48. Savader SJ, Benenatyi JF, Venbrux AC, et al: Choledochal cysts: Classification and cholangiographic appearance. *Am J Roentgenol* 156:237, 1991.
49. Elton E, Hanson BL, Biber BP, et al: Dilated common channel syndrome: Endoscopic diagnosis, treatment, and relationship to choledochocele formation. *Gastrointest Endosc* 47:471, 1998.
50. Caroli J: Disease of the intrahepatic biliary tree. *Clin Gastroenterol* 2:147, 1973.
51. Miller WJ, Sechtin AG, Campbell WL, et al: Imaging findings in Caroli's disease. *Am J Roentgenol* 165:333, 1995.
52. Tsuchida Y, Sato T, Sanjo K, et al: Evaluation of long-term results of Caroli's disease: 21 years' observation of a family with autosomal "dominant" inheritance, and review of the literature. *Hepatogastroenterology* 42:175, 1995.
53. Dayton MT, Longmire WP, Tompkins RK: Caroli's disease: A premalignant condition? *Am J Surg* 145:41, 1983.
54. Sherlock S, Dooley J: Cysts and congenital biliary abnormalities. In Sherlock S, Dooley J, editors: *Diseases of the liver and biliary system,* ed 10, Oxford, 1997, Blackwell, p 579.
55. Choi BI, Yeon KM, Kim SH, et al: Caroli disease: Central dot sign in CT. *Radiology* 174:161, 1990.
56. Takatsuki M, Umemoto S, Inimata Y, et al: Living-donor liver transplantation for Caroli's disease with intrahepatic adenocarcinoma. *J Hepatobiliary Pancreat Surg* 8:284, 2001.
57. Meier C, Deutscher J, Müller S, et al: Successful liver transplantation in a child with Caroli's disease. *Pediatr Transplantation* 12:483, 2008.

Choledochal Cyst

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INTRODUCTION

History and Definition

Douglas[1] reported the first authentic case of choledochal cyst in 1852. Choledochal cysts are uncommon anomalies of the biliary system characterized by localized cystic or fusiform dilatation of the common bile duct with or without intrahepatic biliary dilatation and are associated with pancreaticobiliary maljunction (Figure 1). The wall of the cyst is usually thickened and dense connective tissue, fibrocollagenous and sometimes smooth muscle and elastic elements, are encountered.

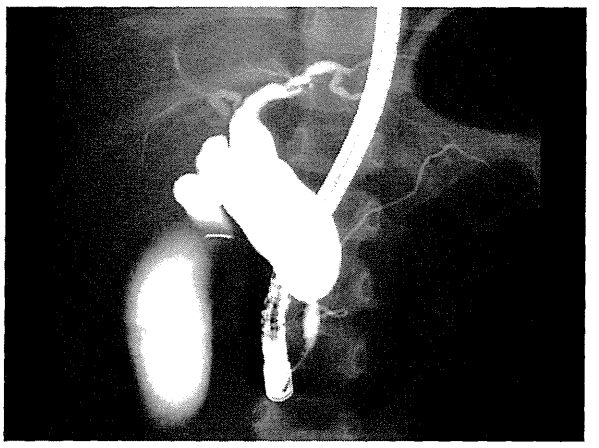

Figure 1. Characteristic image of a choledochal cyst by endoscopic retrograde cholangiopancreatography characterized by bile duct dilatation and pancreaticobiliary maljunction.

Pancreaticobiliary maljunction is a congenital anomaly defined as an abnormal connection between the pancreatic and common bile duct that is located outside the duodenal wall and usually forms a markedly long common channel (≥15 mm).[2] Kozumi and Kodama[3] first conducted a detailed analysis of pancreaticobiliary maljunction in an autopsy case with a choledochal cyst in 1916. However, pathologists and physicians did not pay attention to this anomaly for many years. Babbitt[4] reported 3 patients with pancreaticobiliary maljunction along with his concept of the etiology and pathophysiology of choledochal cyst in 1969. Since Komi et al[5] introduced Babbitt's article, many physicians have paid attention to relations between choledochal cysts and pancreaticobiliary maljunction.

Incidence

Choledochal cysts had been generally considered rare, but recently the number of cases reported in the literature has steadily increased. The incidence of choledochal cysts in Western countries is 1 in 50,000–2,000,000 live births.[6] However, choledochal cysts are not uncommon in Asia and a marked prevalence has been seen in the Japanese population with an incidence of 1 in 1,000.[7] The preponderance of female patients is well known, with the female-to-male ratio being 3 or 4 to 1.[7] Choledochal cysts are found at any age, but almost half of the cases are in children younger than 10 years.

EMBRYOLOGY

Mechanism of Bile Duct Dilatation in Choledochal Cysts

Many theories have been proposed to explain the origin of bile duct dilatation; narrowing of the common bile duct from below by persistence of fetal physiologic epithelial occlusion an obstruction localized at the junction of the bile duct and the pancreas, such as an abnormal angularity or congenital stenosis of the terminal common bile duct. In addition, there is another theory which is the inequality of proliferation of the epithelial cells of the proximal portion in the primitive stage of the common bile duct with proliferation of the cells of the upper segment and less proliferation of the lower portion. The result is that the upper part of the duct becomes abnormally wide and the lower part relatively narrow.[8] However, the mechanism of bile duct dilatation remains uncertain. Amylase is not a causative factor of bile duct dilatation with structural weakening of the wall of the bile duct and then secondary dilatation.

Embryogenesis of Pancreaticobiliary Maljunction

Pancreaticobiliary maljunction is thought to develop as a misarrangement of the embryonic connections in the pancreaticobiliary ductal system, with the terminal bile duct joined to the second branch of the ventral pancreas.[9] During the development of the bile duct, abnormal fusion may occur between the bile duct and branches of the right ventral pancreatic duct. The site in the bile duct where a branch of the pancreatic duct joins it is likely to develop atresia due to disturbance of the recanalization process.[10] However, the embryogenesis of pancreaticobiliary maljunction remains obscure because observation of the fetal development of this anomaly is extremely difficult, and also there is a lack of suitable animal models.

CLASSIFICATION

Classification of Cystic Disorders of the Bile Duct

In 1959, Alonso-Lej et al[11] classified extrahepatic bile duct cysts into 3 types: type I is congenital cystic dilatation of the common bile duct where the intrahepatic tree is usually normal; type II, congenital diverticulum of the common bile duct; type III, choledochocele, a cystic dilatation of the distal segment of the common bile duct protruding into the duodenal lumen. Alonso-Lej's classification, however, did not include intrahepatic bile duct dilatation or pancreaticobiliary maljunction. Todani et al[12] refined the classification of bile duct cysts into 5 types and included the concept of pancreaticobiliary maljunction (Figure 2). Type IV-A is a choledochal cyst complicated by intrahepatic duct dilatation. Type V is single or multiple intrahepatic duct dilatations. Pancreaticobiliary maljunction is not included with type II, type III and type V. Therefore, in a narrow definition, choledochal cyst involves only type I (except type Ib) and type IV-A. Choledochal cysts have been subdivided into those exhibiting cystic, cylindrical, or fusiform dilatation of the common bile duct. However, there is no difference in symptoms, signs, complications, or surgical care among these types. Consequently, there is little point in dividing choledochal cysts into several types by the degree of expansion of the bile duct.

Forme Fruste Choledochal Cyst (Pancreaticobiliary Maljunction without Biliary Dilatation)

Lilly et al[13] in 1985 coined the term '*forme fruste* choledochal cyst' which has the characteristic features of a choledochal cyst except for the cystic component. The first report of a case of choledochal cyst with minimal dilatation of the cyst was by Okada et al[14] in 1981 and it was called the 'common channel syndrome'. Now, *forme fruste* choledochal cyst is known as a variant of a choledochal cyst that has minimal or no dilatation of the extrahepatic bile duct (Figure 3). In Japan, these cases are called 'pancreaticobiliary maljunction without biliary dilatation'. However, it is not so easy to distinguish between a true choledochal cyst and the *forme fruste* because the definition of common bile duct dilatation is not clear.

Forme fruste is considered extremely rare in infants and children, though it is found more frequently in adults. If dilatation of the common

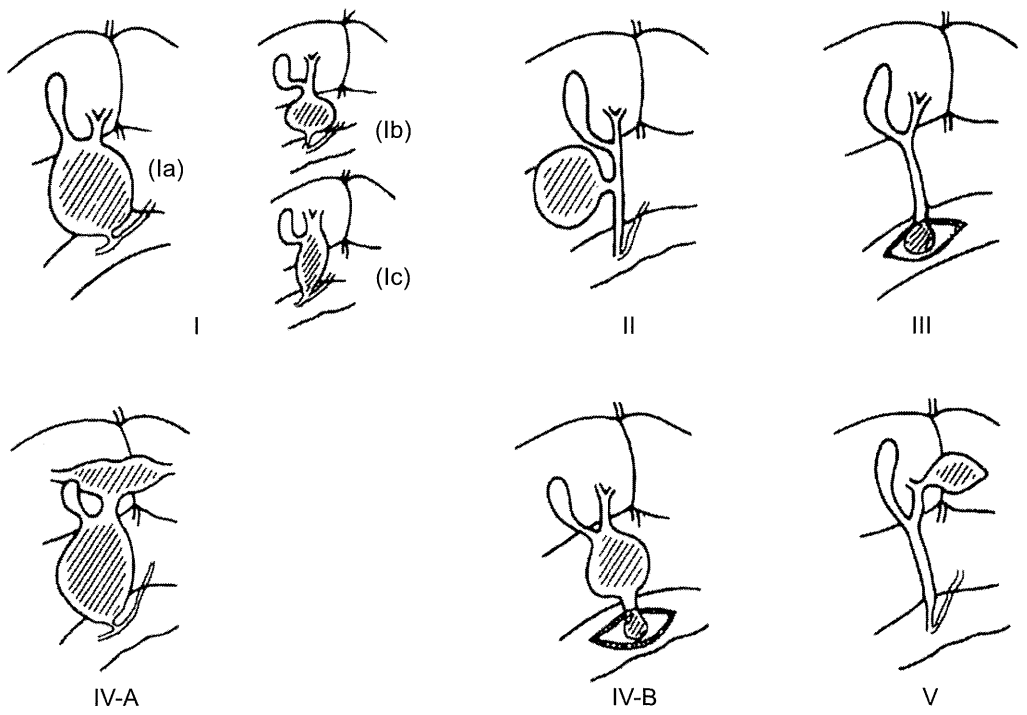

Figure 2. Todani's classification of cystic disorders of the bile ducts.

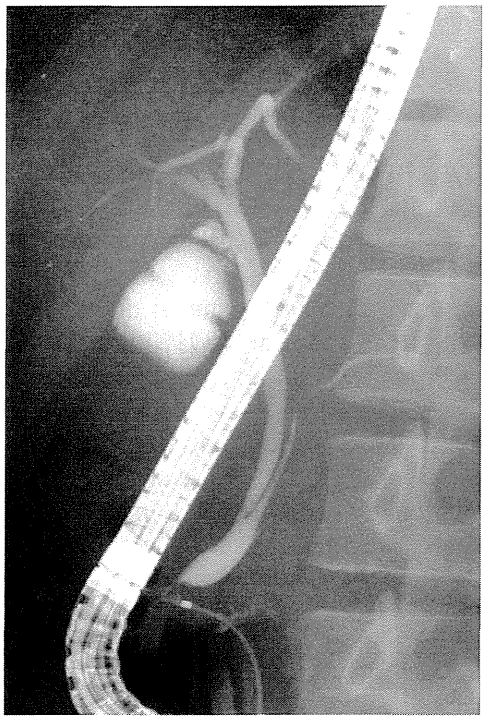

Figure 3. Pancreaticobiliary maljunction without biliary dilatation (forme fruste choledochal cyst).

bile duct is not identified by ultrasonography and endoscopic retrograde cholangiopancreatography (ERCP) is not performed, this type is easily overlooked. According to a nationwide survey in Japan, cases of pancreaticobiliary maljunction without biliary dilatation in adult were 20.3% (514 cases) in patients with pancreaticobiliary maljunction (2,529 cases) and in children they were only 2.7% (68 cases).[15]

PATHOPHYSIOLOGY

As the action of the sphincter of Oddi does not functionally affect the junction of the pancreas and bile duct, two-way regurgitation occurs with pancreaticobiliary maljunction: regurgitation of pancreatic juice into the bile duct, and regurgitation of bile juice into the pancreatic duct. This two-way regurgitation brings about various pathological changes in the biliary tract and in the pancreas.[16]

Bile containing regurgitated pancreatic juice has been reported to produce substances hazardous

to the biliary epithelium, including activated pancreatic enzymes, lysolecithin, secondary or unconjugated bile acids and mutagens.[17] These agents may injure the epithelium of the biliary tract and induce metaplasia or promote cancer. The incidence of epithelial hyperplasia of the gallbladder associated with pancreaticobiliary maljunctions reportedly ranges from 39% to 63%. K-ras mutations in the noncancerous gallbladder epithelium have been detected in 22–50% of the patients with pancreaticobiliary maljunction. Molecular abnormalities of the biliary epithelium include activating the K-ras point mutation and TP53 inactivation. The K-ras mutation occurs early in multistage carcinogenesis, and TP53 inactivation occurs relatively late.[18] Speeding up of the cell cycle, hyperplasia, and K-ras mutation begin during childhood. Various oncogenic factors have been implicated in biliary carcinogenesis in patients with choledochal cysts. Although carcinogenesis in the cystic lesions is not yet fully understood, cholestasis and recurrent cholangitis may play an important role in provoking malignant change of the biliary epithelium.

SIGNS AND SYMPTOMS

The classical triad of abdominal pain, jaundice, and an abdominal mass was originally described as the key features of choledochal cysts, but now it is present in fewer than 20% of patients.[19] Major clinical symptoms with choledochal cysts in children are recurrent abdominal pain (81.8%) that may occur repeatedly for several days, nausea and vomiting (65.5%), mild jaundice (43.6%), an abdominal mass (29.0%), and fever (29.0%).[20] Abdominal pain is the most frequent symptom in adult, but it is nonspecific, and one third of adults are asymptomatic.[21] Other common symptoms in adult are jaundice, vomiting, and fever. Pancreatitis may be one of the other major presentations in adults. However, acute pancreatitis is observed more frequently in children from 1 to 15 years of age (70.6%) than in adults (18.6%). Meanwhile, symptoms of *forme fruste* cysts in children include recurrent abdominal pain, jaundice, fever, and pancreatitis and these closely resemble those seen in patients with choledochal cysts.

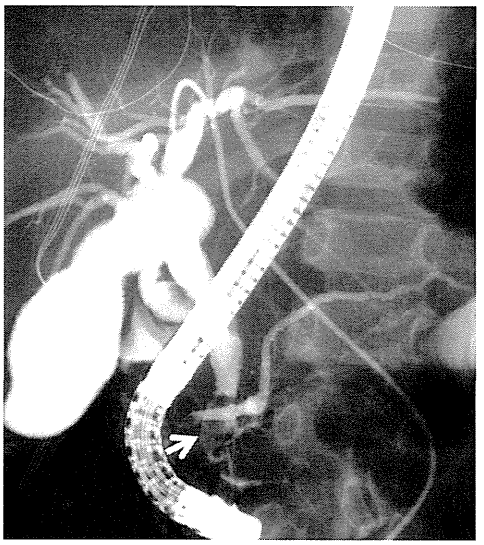

Figure 4. Protein plugs incarcerated in the common channel (arrow).

The occurrence of these symptoms may be explained by the disturbance in bile and pancreatic secretory flow caused by protein plugs, which resolve spontaneously.[20] Protein plugs are compacted in the common channel, obstruct the bile and pancreatic ducts, and increase intraductal pressure, resulting in these symptoms (Figure 4). Intermittent symptoms may be due to repeated plug formation.

DIAGNOSIS

Biochemical Examination

There are no specific laboratory tests to identify choledochal cysts, but patients sometimes show abnormal levels of serum bilirubin, serum amylase, lipase, and transaminases. Pancreatic enzymes, especially amylase, in the bile within the bile duct and gallbladder are generally present at extremely high levels of 20,000–200,000 IU/L.[22] An elevated level of amylase in the bile seems to be a useful biochemical marker of pancreatic reflux into the bile duct. However, the pancreatic amylase activity in newborns is 3% of that of adults, begins to increase at 7–8 months, and reaches adult values by 5 years. Therefore, the amylase level in the bile of very young children appears not to be a reliable biochemical marker of pancreatic reflux. Recently, it

has become obvious that these refluxes can occur in individuals without pancreaticobiliary maljunction. It is called high confluence of pancreaticobiliary ducts in which the common channel is at least 6 mm long and the effect of the sphincter does reach the pancreaticobiliary junction.[23] In addition, pancreaticobiliary reflux can also occur in cases of sphincter dysfunction, periampullary diverticula, and after endoscopic sphincterotomy or endoscopic papillary balloon dilatation.

Diagnostic Imaging

The non-invasiveness and accuracy of ultrasonography support its use as the initial investigative procedure. Ultrasonography clearly identifies the dilated common bile duct, and shows biliary sludge or stones within the cyst in some cases. Focal thickening of the cyst wall raises the suspicion of a carcinoma.

Radiographic visualization of both the biliary tree and pancreatic duct prior to surgery is helpful for the surgical manipulation and complete excision of the cyst. Endoscopic retrograde cholangiopancreatography particularly provides an excellent visualization of the cyst, duct anatomy, and pancreaticobiliary maljunction. Endoscopic retrograde cholangiopancreatography provides characteristic images of choledochal cysts: localized cystic dilatation involving the common bile duct, stenosis at the lower portion of the cyst, abnormal junction of the pancreatic and bile ducts away from the papilla, dilated common channel, normal dorsal pancreatic duct, dilated cystic duct, and stenoses at the hepatic ducts (Figure 1). This examination is important in order to avoid intraoperative injury of the pancreatic duct and to recognize protein plugs within the common channel. However, ERCP is invasive and associated with a small risk of complications such as iatrogenic pancreatitis and acute cholangitis. Additionally, ERCP must be performed under general anesthesia in children.

A new imaging technique, endoscopic ultrasonography (EUS), allows adequate visualization and high-resolution imaging of the pancreatobiliary region.[24] The muscularis propria of the duodenum and pancreatic parenchyma can be examined by EUS, confirming that the pancreaticobiliary junction lies outside the duodenal wall irrespective of the length of the common channel (Figure 5). Endoscopic ultrasonography is helpful in diagnosing gallbladder cancer, choledocholithiasis, acute pancreatitis and choledochal cysts as well as pancreaticobiliary maljunction. It is a safer imaging technique than ERCP and can be performed in outpatients; however, it must be performed by an experienced specialist as its diagnostic accuracy is operator-dependent.

Endoscopic ultrasonography has major complications, e.g. esophageal perforation, pharyngeal and duodenal perforation, and bleeding, in around 0.05%.

Magnetic resonance cholangiopancreatography (MRCP) can play an important role as a non-invasive examination without radiation exposure and should be considered a first-choice imaging technique for evaluation of choledochal cysts (Figure 6). Magnetic resonance cholangiopancreatography appears to offer diagnostic information for assessment of choledochal cysts in adults and provides a non-invasive method that is particularly advantageous in postoperative patients, and may be an efficacious alternative to ERCP.[25] Its greatest strength compared with computed tomography (CT) is its availability for biliary obstructed patients such as patients with severe jaundice and protein plugs.[26] However, MRCP often fails

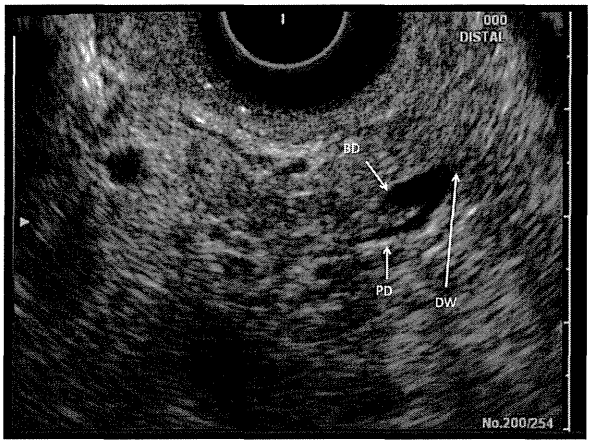

Figure 5. Endoscopic ultrasonography findings of pancreaticobiliary maljunction. The pancreatic duct (PD) and bile duct (BD) join anatomically outside the duodenal wall (DW).

to provide clear imaging in children due to the difficulty of their holding their breaths.

Computed tomography combined with intravenous cholangiography is useful for the demonstration of a cyst or postoperative evaluation for intrahepatic bile ducts and bilioenteric anastomoses. The great advantage of CT is its ability to produce high-quality images without respiratory artifacts and to provide more anatomical detail of the biliary tract.[27] Helical CT cholangiography is useful for identifying the anastomotic site of hepaticojejunostomy and hepatic ductal stenosis during postoperative follow-up.[28] Three-dimensional CT is useful for delineating the positions of the intrahepatic biliary branches and detecting biliary stenoses.

Prenatal Diagnosis

The first case of an antenatally diagnosed choledochal cyst by ultrasonography was reported in 1980, and since then the number of cases of choledochal cysts diagnosed prenatally has increased.[29] However, the ratio of cases diagnosed prenatally is ≤5% of all cases of choledochal cysts. There is a report of a diagnosis in the 15th week; however, most of the cases are detected during the second or third trimester (4–6 months).[30] It is interesting to note that most of these cysts are of large size, and there are no reports of fusiform choledochal cysts detected prenatally.[30]

The diagnosis is suggested by the presence of a cyst having a size of 2–3 cm in the subhepatic area in an examination for fetus ultrasonography or magnetic resonance imaging (MRI) (Figure 7). The differential diagnosis of such a cystic mass on the right side of the abdomen includes duodenal atresia, ovarian cyst, enteric duplication cyst, meconium pseudocyst, mesenteric cyst, hydronephrosis, and biliary atresia.[31] Particularly, cystic biliary atresia (type I cyst) is important in the differential diagnosis of a choledochal cyst on antenatal ultrasound scan or MRI, and children with presumed choledochal cysts should undergo early exploration to rule it out.

COMPLICATIONS

Cholelithiasis

Cholelithiasis is the most frequent complication associated with choledochal cysts. The prevalence of intracystic stones ranges from 9.0% in children to 24.1% in adults, with the stone site being in the gallbladder in 12.7%, bile duct in 65.8%, and liver in 21.5% of cases.[9] A nationwide survey in Japan collected 1947 cases (950 children and

Figure 6. Magnetic resonance cholangiopancreatography findings of a choledochal cyst.

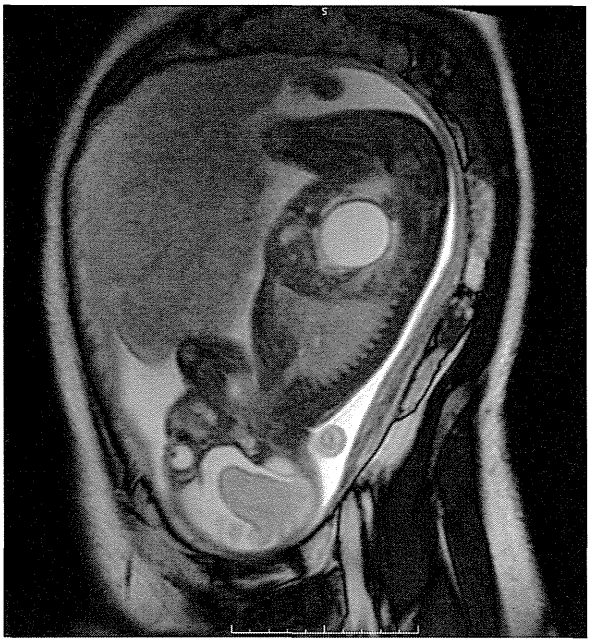

Figure 7. Fetal common bile duct. A round cystic mass is recognized in the subhepatic area.

997 adults) and reported a higher incidence of gallstones in adults than children (23.3% vs 9.5%).[15]

Pancreatitis

The frequency of acute pancreatitis in children with choledochal cysts is reportedly 68% and ranges from 18% to 23% in adults.[32] However, acute pancreatitis associated with a choledochal cyst is usually mild and recurrent without extrapancreatic spread or pancreatic fluid collection. During an attack of acute pancreatitis, protein plugs obstruct the common channel by a ball valve mechanism, and provoke increased intraductal pressure of the pancreaticobiliary ducts.[33] Most protein plugs are fragile and disappear spontaneously because they consist of >98% of protein, which explains the self-limiting nature of the symptoms.[33] Radiolucent filling defects consisting of protein plugs were detected in a common channel in 40% of patients with choledochal cysts[20] (Figure 4).

Pancreatitis is treated conservatively by fasting. However, some protein plugs do not disappear but exacerbate symptoms, requiring biliary drainage for symptomatic relief. Endoscopic drainage is thought to be an effective pre-operative treatment when pancreatitis is uncontrollable by medical therapy and is induced by protein plugs in the dilated common channel.

Spontaneous Perforation

Dijkstra[34] reported the first case of the spontaneous perforation of the bile duct in 1932. Lilly et al[35] in 1974 described a series of 53 cases collected from the world literature and Yamaguchi[7] reported a collection of 26 Japanese cases in 1,433 patients with choledochal cysts (1.8%). Spontaneous perforation of the bile duct is uncommonly encountered in infancy. However, this is one of the complications of the choledochal cyst. The exact cause of perforation still remains uncertain. Some authors believe that irritation from refluxed pancreatic juice coupled with an immature bile duct wall is responsible for the spontaneous perforation of the bile duct, and it may be the result of the acute increase in intraluminal pressure by the protein plugs.[36,37]

Spontaneous perforation of the bile duct may manifest clinically as an acute abdomen with bile peritonitis but many patients do not present with typical signs of overt peritonitis. Abdominal guarding and rebound tenderness are not apparent in many cases. Bile peritonitis is usually a sterile chemical inflammation and may not create signs similar to bacterial peritonitis secondary to bowel perforation. Hence, the abdominal signs and symptoms are nonspecific. The serum bilirubin is not markedly elevated possibly as a result of rupture leading to partial decompression of the biliary system.[37,38] As mentioned above, spontaneous perforation of the bile duct can be a diagnostic challenge because the clinical presentation is often nonspecific. However, ultrasonography, MRI or CT can diagnose it without much difficulty. Peritoneal free fluid with dilated bile ducts is very suggestive of spontaneous perforation.

Carcinoma

It is well-known that a choledochal cyst has a significant association with biliary tract carcinoma.[12] However, no attention was paid to this previously. Irwin and Morison[39] described the first reported malignancy associated with a choledochal cyst in 1944. Malignant transformation might develop mainly in the gallbladder and bile duct, because the biliary epithelium is influenced by both bile stasis and activated pancreatic juice. According to a nationwide survey performed in Japan, cancer of the biliary tract was found in 21.6% of 997 patients with choledochal cysts in adulthood and was in the extrahepatic bile duct in 32.1% and gallbladder in 62.3%.[15] This is significantly higher than the 0.01–0.05% incidence of bile duct cancer in the general population. The incidence of bile duct cancer increases with age from 2% for patients in their 20s to 43% for those in their 60s.[40] In addition, gallbladder cancer is often associated with *forme fruste* cysts and was detected in 37.4% of 514 adult patients[15] (Table 1).

The presence of carcinoma in a choledochal cyst is mainly found in adult patients. However, carcinoma of patients with choledochal cysts also tends to occur in the younger age group (younger than 15 years old) and 9 cases of biliary tract

Table 1.
Incidence of Biliary Tract Cancer in Adult Choledochal Cysts

	Choledochal cyst	Pancreaticobillary maljunction without billary dilatation
Number of patients	950	514
Biliary tract cancer (%)	215 (21.6)	218 (42.4)
Location		
Gallbladder	134 (62.3)	192 (88.1)
Bile duct	69 (32.1)	16 (7.3)
Gallbladder and bile duct	10 (4.7)	9 (4.1)
Unknown	2 (0.2)	1 (3.9)

cancer have been reported in Japan. The youngest reported to have adenocarcinoma arising in a choledochal cyst was a 3-year-old boy.[41] Therefore, once the diagnosis of choledochal cyst is made, early radical surgery should be performed, irrespective of the patient's age.

TREATMENT

History

The first successful report of treatment was a case who had a cholecystojejunostomy by Swain et al in 1894 and the next successful report was a choledochocystojejunostomy in 1897. Internal drainage had previously been performed commonly as a safety treatment of choledochal cyst to relieve stagnation of bile flow. Early reports suggested that internal drainage (e.g., cystoenterostomy) was satisfactory surgical treatment. However, drainage procedures have been abandoned because of the high rate of complications by choledocholithiasis and biliary malignancy.[42] Todani et al[43] reported that patients with previous internal drainage developed cancer at a mean age of 35.6 years, approximately 10 years after cystojejunostomy or cystoduodenostomy. This average age was thought to be 15 years earlier than that of patients with cancer who had not undergone previous drainage surgery. Therefore, internal drainage augmented the risk of malignant change despite alleviation of cholestasis.

Kasai et al[44] in 1970 reported that choledochal cysts should be removed and replaced by a hepaticojejunostomy in a Roux-en-Y fashion, even in children, to reduce postoperative morbidity and prevent cancer. Prophylactic biliary diversion surgery became the standard operation for choledochal cysts, because it stopped the reflux of pancreatic juice through pancreaticobiliary maljunction.[45] This surgical procedure, of bile duct resection and bilioenteric anastomosis is referred to as the 'separation-operation'.

Operative Procedures for Choledochal Cysts

Complete excision of the extrahepatic bile duct has been widely adopted as the standard treatment of choledochal cysts. The aim of this operation is to excise both the common bile duct and the gallbladder, where malignancy may arise, and to prevent both bile stasis and the reflux of pancreatic juice into the bile duct.

First, the gallbladder is mobilized then, dissection of the intrapancreatic cyst proceeds on the outer plane of the epicholedochal plexus where only loose fibrous tissue exists so as to leave the plexus with the cyst wall.[46] For the resection of the cyst, there are some other methods. In Lilly's method the cyst wall is incised transversely at first and a plane of dissection is selected in the posterior wall which will separate it into a thin outer and thick inner layer[47] (Figure 8). After completing the separation, the inner wall is