Management Dilemmas With Choledochal Cysts

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Context: Choledochal cysts are rare and of unknown cause. Their presentation is protean, with the classical triad of pain, jaundice, and mass rarely seen. The potential complications are serious, including pancreatitis, cholangitis, and cholangiocarcinoma.

Objective: To present the current experience and evidence relating to all aspects of choledochal cysts to derive appropriate management recommendations.

Methods: Review of relevant literature in the English language indexed on MEDLINE.

Results: The elaboration of the classification of choledochal cysts. We describe the modes of presentation and optimal investigation and summarize the current theories on etiology and malignant transformation. The results of different management strategies are presented.

Conclusions: Choledochal cysts are often detected during the investigation of nonspecific symptoms, or even incidentally detected. Magnetic resonance imaging is the best imaging modality for the diagnosis and characterization of these cysts. Complete excision and hepaticojejunostomy is the management of choice.

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Choledochal cysts are uncommon and of unknown cause, with an incidence of 0.1% even among adults referred for endoscopic retrograde cholangiopancreatography (ERCP) investigation. In a pediatric surgical unit in Spain, only 0.03% of the cases were for choledochal cyst disease. There is a higher incidence in females and they are more common in the Far East than in populations of Western European origin. The presentation is often vague and nonspecific, impeding prompt diagnosis. However, the diagnosis is facilitated by modern imaging techniques, and may be made at any time from the antenatal period to adult life. While some aspects of optimal management have been resolved, others remain controversial. The more severe complications of choledochal cyst disease include pancreatitis, cholangitis, biliary cirrhosis, and cholangiocarcinoma. This review considers the literature on choledochal cysts, concentrating particularly on current issues in management of the disease.

Classification

The most commonly used classification, developed by Alonso-Lej et al and modified by Todani et al, describes 5 broad types of choledochal cysts. The 2 relatively common categories of cyst are types I and IV-A. Type I, the most commonly reported overall, consists of dilatation of the common bile duct, which may be cystic, focal, or fusiform (subtypes A, B, and C, respectively). Type IV-A cysts are the second most common, defined as both intra- and extrahepatic dilatation of the biliary tree. The remaining types are considerably rarer, with no large series published, and only sporadic reports appearing in the literature. Type II describes a saccular diverticulum off the common bile duct. Type III is represented by a cystic dilatation of the intramural portion of the common bile duct and is contended by some to represent a duodenal diverticulum rather than a choledochal cyst in view of the anatomical location and the duodenal epithelium with which they are always lined. The rare malformation of multiple extrahepatic cysts is designated type IV-B. Type V is synonymous with Caroli disease, describing multiple intrahepatic biliary dilatations.

Etiology

The most commonly propounded theory for the etiology of choledochal cysts re-
lates to the observation that they are often associated with an anomalous pancreatobiliary junction with a long common channel (>15 mm). This is purported to allow pancreatic juice to reflux into the biliary system and to cause increased pressure within the common bile duct, which, in combination, may cause ductal dilatation. More recently, abnormal function of the sphincter of Oddi has been reported to predispose to pancreatic reflux into the biliary tree, and spasm of the sphincter of Oddi has been noted to be associated with choledochal cysts. Animal models demonstrating progressive dilatation of the common bile duct following anastomosis of the common bile duct to the pancreatic duct support this theory. However, the possibility that such challenging surgery may result in at least partial obstruction of the biliary system, and that in fact obstruction causes the dilatation rather than pancreatic juice reflux, cannot be entirely discounted. There is also some clinical evidence suggesting that anomalous pancreaticobiliary duct union is not responsible for choledochal cysts, at least not entirely.

First, anomalous pancreaticobiliary union is detected in 57% to 96% of cases of choledochal cyst, and therefore cannot account for the minority of cases with normal ductal entry into the ampulla of Vater. Second, it seems that choledochal cysts diagnosed antenatally do not have pancreatic juice reflux into the common bile duct, and that the concentration of biliary amylase rises with age at presentation, increasing the possibility that the reflux may occur in part as a result of choledochal cysts, but not necessarily as the cause. Another study of children with choledochal cysts found that 10 of 24 children had no activation of pancreatic enzymes in the common bile duct, and of these, 8 were younger than 2 months; therefore, pancreatic reflux is an unlikely candidate for the cause of these choledochal cysts.

Second possible cause of choledochal cysts has already been alluded to, in suggesting an alternative interpretation of the animal experiments anamomosing the common bile duct to the pancreatic duct as discussed previously. Obstruction of the common bile duct is another etiological theory for choledochal cysts and is also supported by other animal models. In neonatal animal models, ligation of the common bile duct causes a dilatation morphologically resembling a type I choledochal cyst; whereas in adults, generalized dilatation of the whole biliary system can be seen. Clinically, there is some evidence to support the theory that obstruction of the distal common bile duct may cause choledochal cyst. A case report of an antenatally diagnosed choledochal cyst found complete distal obstruction of the lower end of the common bile duct. Another case report found a congenital web at the lower end of the common bile duct in association with a type I choledochal cyst. The abnormal function of the sphincter of Oddi, reported in some studies to be associated with choledochal cysts, may represent a functional obstruction to the common bile duct, thus predisposing to choledochal cysts. This functional obstruction at the sphincter of Oddi also predisposes to pancreatic juice reflux into the biliary tree.

These putative causes are not necessarily contradictory, as a distal common duct obstruction may coincide with an anomalous pancreaticobiliary union. It is conceivable that when such a coincidence occurs, both mechanisms act in tandem.

Some further observations have been made, which may be relevant to the etiology of choledochal cysts. One such observation is that the distal common bile duct has inadequate autonomic innervation. Kusunoki et al showed that there are abnormally few ganglion cells in the narrow portion if the common bile duct in patients with a choledochal cyst, as compared with controls. Presumably, this would result in a functional obstruction and proximal dilatation in the same manner as achalasia of the esophagus or Hirschprung disease.

Real-time polymerase chain reaction has been used to demonstrate high levels of reoviral RNA in biliary tissues from patients with choledochal cysts compared with controls. It is possible only to speculate as to how this may result in choledochal cysts. Perhaps viral infection of ganglion neurons causes the oligoganglionosis as discussed above, and perhaps viral infection triggers an immune response, which is subsequently responsible for fibrosis of the lower end of the biliary tract.

There are few reports of familial cases of choledochal cysts and associated anomalies. A pair of monozygotic twins were discordant for the occurrence of anomalous pancreatobiliary junction and choledochal cyst, suggesting that there is not a strong genetic basis for these malformations. However, there may be some genetic predisposition, as there are reports of a mother and daughter and of dizygotic twins having choledochal cysts. Interestingly, in both reports, the cysts are of different Todani types; therefore, if there is a genetic basis for the predisposition in the families described, then it would seem to affect the biliary tree globally.

On balance, the weight of the evidence seems to support distal common bile duct obstruction (either anatomical or functional) and raised intraductal pressure as the most likely cause of choledochal cysts. The high incidence of anomalous pancreatobiliary union cannot be ignored, but may just reflect an association with distal obstruction. Alternatively, pancreatic juice reflux into the common bile duct may be activated by bile, and activated enzymes subsequently weaken the common bile duct wall, exacerbating the dilatation.

Type IV-A cysts are more common in adults than in children, raising the possibility that although the lesions may be congenital, they may progress with time.

### PRESENTATION

The classical triad of jaundice, right upper quadrant mass, and abdominal pain is present in only a minority of patients (0%-17%). It is more commonly seen in cases with onset in childhood rather than in adults, and 85% of children have at least 2 features of the triad at presentation, compared with only 25% of adults.

Antenatal diagnoses can be made on ultrasound, although diagnostic accuracy from this technique has been reported to be as low as 15%, and it is not possible to differentiate between biliary atresia and choledochal cysts with antenatal ultrasound. Although 1 of 2 case reports suggests that serial antenatal ultrasound may permit the differential according to relative rates of enlarge-
impact with proximal dilatation has been reported to operatively, owing to the quality of modern imaging. Stone adults, the diagnosis is only sporadically in doubt preperitonitis from cyst rupture. Among adults, choledochal cysts are quite often incidental findings during investigation for other problems. The presentations of choledochal cysts are clearly protean, and prompt diagnosis relies on a high index of suspicion, aided by modern imaging techniques. Foremost among the differential diagnoses of dilatation of the common bile duct in children is biliary atresia. In adults, the diagnosis is only sporadically in doubt preoperatively, owing to the quality of modern imaging. Stone impaction with proximal dilatation has been reported to mimic choledochal cysts. One adult thought to have a pancreatic pseudocyst was found to have a choledochal cyst at operation; this is easy to understand in view of the high incidence of pancreatitis caused by choledochal cysts. Another case report mistook primary sclerosing cholangitis for a choledochal cyst. INVESTIGATION Ultrasound Scanning Ultrasound can diagnose choledochal cysts with a specificity of 97% in children, although this drops to 71% if the width criteria are reduced to increase sensitivity, with normal variants and secondary causes of biliary dilatation being misdiagnosed as choledochal cysts. Another study found that ultrasound successfully diagnosed 15 of 19 children younger 6 months with choledochal cysts. Ultrasound is therefore an excellent first-line investigation of neonatal jaundice persisting more than 2 weeks after birth and may help to differentiate choledochal cysts from biliary atresia. Radionuclide Scintigraphy Scintigraphy is safe and atraumatic, and has been used for a long time in the diagnosis of choledochal cysts. Following the progression of an isotope from the biliary tract into the small intestine is reported to distinguish with 100% accuracy between choledochal cysts and biliary atresia. Type 1 cysts may be diagnosed with a sensitivity of 100%, but only two thirds of type IV disease is detected, and the extent of the intrahepatic disease may be underestimated on scintigraphy. Computed Tomographic Scan Although there are reports of computed tomographic (CT) scans diagnosing choledochal cysts, others have found that cysts are missed on CT scans, and picked up on magnetic resonance cholangiopancreatography (MRCP). A comparative study of 14 patients with choledochal cysts was performed, in which each patient had both CT cholangiography and MRCP performed. The MRCP investigation was superior at detecting and defining lesions. A better role for CT scanning may be in the postoperative period, where it was shown to be superior to MRCP in locating the biliary-enteric anastomosis and in defining any stenosis thereof. Endoscopic Retrograde Cholangiopancreatography Investigation with ERCP is an excellent tool for defining biliary anatomy, and as such has been used to diagnose choledochal cysts. However, MRCP has been shown to be just as good as, if not better than, ERCP, without the potential complications of the latter, invasive technique. Magnetic Resonance Cholangiopancreatography For the reasons outlined above, MRCP represents the current "gold standard" in the imaging of choledochal cysts. There are a few caveats to this. Although the technique is excellent for diagnosing and characterizing the cysts themselves, it is not so good at detecting anomalous pancreaticobiliary union. This is probably not all that important in determining patient management. Also, MRCP may not be as sensitive a tool in pediatric cases as it is in adults, where ultrasound has a preeminent role. COMPLICATIONS Pancreatitis This is quite a common presentation of choledochal cysts, as described earlier. This may be due to the activation of pancreatic enzymes by bile reflux, in association with an anomalous pancreaticobiliary union. Certainly, the anomalous ductal union seems to predispose to pancreatitis, as in one study, 57% of patients with choledochal cysts had anomalous ductal union demonstrated by ERCP. All of these patients suffered pancreatitis. Only a third of patients with normal ducts had pancreatitis. Cholangitis As with pancreatitis, cholangitis is a common complication of choledochal cysts and may be the presenting feature as mentioned earlier. It is also a commonly reported complication after surgical management. Biliary Cirrhosis This has been reported to be the presenting feature in 10% of children in one series, and in biopsies obtained during surgery, it has been found to occur in 40% to 50% of cases. In one series, liver changes, including bile duct proliferation, cholestasis, parenchymal damage, inflammatory cell infiltration, and pericentral fibrosis, were present in all livers on which biopsies were performed, irrespective of liver function and macroscopic liver appearance.
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and 30%, 18,42,78-80 Malignant change in association with

choledochal cysts has been reported in pediatric cases, and it should therefore be suspected in any choledochal
cyst appearing after infancy.

The pathogenesis of cholangiocarcinoma in chole-
dochal cysts may be caused by the carcinogenic effect of

pancreatic reflux. Supporting this contention is a study

noting that the risk of cholangiocarcinoma in cysts is much

higher in patients with anomalous pancreaticobiliary union

(32%) than in those without (0%). It seems that the pres-

ence of anomalous ductal union may be even more

important than that of choledochal cyst, as one study found

a 55% rate of biliary tract malignant neoplasia in patients

with duct malunion, and only a 5% rate in patients with-

out, whether (n=14) or not (n=4) choledochal cyst was present. The incidence of gallbladder carcinoma in pa-

ients with ductal malunion without choledochal cyst was

50% in another study, and only 5% in patients with

malunion and choledochal cysts. In the patients with-

out cysts, all the biliary malignancies were in the gallblad-

der, whereas in the patients with cysts, in addition to the

5% with gallbladder cancer, 14% had cholangiocarci-
noma arising in the cyst.

It has been demonstrated that the histological

changes in choledochal cysts progress with patient age

at presentation, through epithelial denudement to

inflammatory infiltrates, glandular metaplasia, and

ultimately, malignancy.

Putting these findings together, it is conceivable that

pancreatic juice reflux secondary to anomalous ductal

union is the predisposing factor for biliary tract malign-
nancy, and that malignancy occurs in a region of biliary

stasis, where the exposure to the refluxed pancreatic juice

is prolonged. In the presence of a cyst of the common bile
duct, this would be closer to the anomalous ductal union

than the gallbladder, and therefore, more at risk of malig-
nant change. In the absence of a choledochal cyst, the gall-

bladder is the only site of biliary stagnation.

There are some reports of malignant change in cho-

ledochal cysts by Todani classification that are relevant to

management. Although it has been reported that type

III cysts rarely undergo malignant change, there are re-

ports of malignancy arising in choledochocoeles, and in a series of 11 patients with type III cysts, 3 contained

cholangiocarcinoma at the time of diagnosis. In type IV-A
disease, there are reports of malignancy arising in the in-

trahepatic dilated ducts, rather than in the common bile
duct cysts. The management implications of these ob-

servations are discussed in the subsequent section.

MANAGEMENT

Excision vs Internal Drainage Procedures

Historically, a cholecystoenterostomy was considered a surgical management option for choledochal cysts. How-

ever, the most recent articles to advocate this approach were published in the 1970s. This approach has been

abandoned in favor of cyst excision with hepatice-terostomy, to reduce the complications of the former pro-

cedure. These include malignancy in the remaining cyst, pancreatitis, and cholangitis.

When a patient has previously been treated by a cyst-

enterostomy internal drainage procedure, 70% of pa-

tients require reoperation for the occurrence of complica-

tions, including cholangitis and hepatolithiasis. Indeed it has been recommended that patients who have previ-

ously undergone internal drainage procedures should un-

dergo reoperation with cyst excision (even if asymptom-

atic) as prophylaxis against complications in particular

cases of malignant cysts, even though the complica-

tions of surgery for excision after previous internal drain-

age procedure are more frequent than those seen after primary cyst excision.

Timing of Surgery

The timing of surgery should be early after diagnosis to

reduce the incidence of complications described, and

particularly to prevent liver damage in neonates.

Malignant Change After Cyst Excision

Even after cyst excision, there are reports of malignancy

occurring, often relating to incomplete cyst excision.

There is a series dissenting this, with a zero rate of post-

excision malignancy in 37 patients, even though the exci-

sion was known to be incomplete in 28 cases. However, in a comprehensive review, the incidence of

postexcision malignancy has been estimated at 0.7%.

This may occur in the residual intrapancreatic portion

of the choledochal cyst excision. The recognition of this danger has driven the trend toward excision of the intrapancreatic portion of the common bile duct to the point of demonstrating the pancreaticobiliary duct union to ensure complete excision.

The extent of the resection in type IV-A cysts is contro-

versial. Several authors advocate management by ex-

cision of the extrahepatic component only, with hepatic-

centerostomy. However, malignancy has been

reported to arise in the intrahepatic cysts as described above, and it has also been reported to occur after resec-

tion of the extrahepatic cyst with hepatice-terostomy. Clearly, when the intrahepatic cysts are widespread, they cannot be excised; however, when the intrahepatic disease is localized, it would seem reasonable to perform the relevant partial hepatectomy. This approach has been practiced by other authors.

For the same reason, partial hepatectomy has been prac-

ticed for Caroli disease.

There is a report of cylindrical intrahepatic ductal dilatation in type IV-A disease regress-
ously after common duct excision and hepaticojunostomy, compared with cystic intrahepatic disease, which does not regress. However, it seems likely that the cylindrical intrahepatic disease represents a type I cyst with an element of obstruction causing proximal dilatation, rather than a true type IV-A disease.

**Choledochocoeles: An Exception to the Rule?**

The malignant potential of type III cysts has been questioned in a review of 65 choledochocoeles, and for this reason they are often treated as the exception to the rule, by drainage into the duodenum at the ampulla, rather than by excision. The enormous attraction of this approach is that it may be performed endoscopically by sphincterotomy, however, as described above, malignancy does occur in type III cysts, and in one series in 3 of 11 patients. It is perhaps odd then that in the literature there are no advocates for the excision of choledochocoeles.

**Reconstruction of Biliary Drainage**

The most common reconstruction following cyst excision is a hepaticojunostomy or choledochojunostomy, with the former thought to reduce the incidence of stricture formation postoperatively. Alternatives that have been suggested include hepaticoduodenostomy so that the anastomosis is accessible to ERCP in the event of postoperative complications, and hepatocantoctomy apparently for a more physiological result. Neither hepaticoduodenostomy nor hepatocantoctomy have been widely adopted; the former perhaps because there are other ways of providing access to a biliary-enteric anastomosis without the relatively high risk of complications from a duodenal anastomosis. The latter may have had a variety of potential problems if the experience reported following a choledochal cystogastrostomy is anything to go by. The technique of appendix interposition hepatocentoctomy similarly failed to gain widespread acclaim, as the appendix grafts underwent stenosis, and as a result, there was significant hepatic fibrosis secondary to obstruction.

**Postoperative Complications**

Postoperative anastomotic strictures are a common problem and are associated with intrahepatic cholestasis and cholangitis. Intrahepatic stones are particularly a problem in cases of type IV-A disease with residual intrahepatic cysts.

The incidence of anastomotic stricture formation may be reduced by performing a higher anastomosis, as Todani found that 9 of 22 choledochojenuostomies had postoperative anastomotic strictures, compared with 1 of 82 hepaticojunostomies. Cholecodochoscopy at the time of surgery to detect and remove intrahepatic stones at operation reduces postoperative complications of cholestolithiasis. Roux-en-Y limb stomas and access limbs have been used to facilitate endoscopic access to anastomotic strictures.

**Laparoscopic Excision**

Recently, laparoscopic cyst excision and hepaticojunostomy have been described. It is too early to assess the long-term results of this approach in terms of anastomotic strictures and malignancy arising in residual cyst tissue.

**SUMMARY**

Choledochal cysts are uncommon, but when encountered, they may appear nonspecifically rather than classically, and a high index of suspicion will avoid a delay in diagnosis. The imaging modality of choice for diagnosing and characterizing choledochal cysts is MRCP. Delayed diagnosis may have a variety of undesirable sequelae including biliary cirrhosis, cholangiocarcinoma, pancreatitis, and cholangitis. To avoid these complications, choledochal cysts should be treated by complete excision wherever possible, with the possible exception of type III duodenal intramural cysts, which are often treated by endoscopic sphincterotomy. The approaches to intrahepatic disease and postoperative complications have also been discussed.

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