Congenital choledochal malformation: not just a problem for children

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ABSTRACT

Choledochal cysts remain relatively uncommon in Western Europe and the US, although they are appreciably more common in Asia. Their aetiology remains obscure although abnormalities of the pancreaticobiliary junction may be the primary pathology in some, with biliary dilatation following reflux of activated pancreatic secretions. Most anomalies will present in childhood with obstructive jaundice or abdominal pain; a proportion may only present for the first time during adulthood, and some of these will show malignant transformation. The classical triad of pain, jaundice and a palpable mass is, however, not common. Complete cyst excision, where possible, and biliary reconstruction remain the aims for most types although there is still some controversy about the type of reconstruction. Laparoscopic reconstruction is possible but is still very much an advanced technique. The risk of long-term problems post-surgery is significant. Whether this is due to recurrent pancreatitis secondary to the retained common channel and/or a distal stump, or due to the development of biliary tract malignancy is still a cause for concern and indicates the need for adequate, prolonged follow-up.

Abbreviations: CBD, common bile duct; CHD, common hepatic duct; CT, computed tomography; ERCP, endoscopic retrograde cholangiopancreatography; MRI, magnetic resonance imaging; MRCP, magnetic resonance cholangiopancreatography; PTC, percutaneous transhepatic cholangiography

KEYWORDS

Choledochal cyst – Common channel – Biliary tract carcinoma – Hepaticojunostomy

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A choledochal cyst was first noticed by the German anatomist Abraham Vater in 1723.¹ Notwithstanding this, the first detailed case in the English literature was that of Halliday Douglas of Edinburgh who, in 1852, described a 17 year-old girl who had jaundice and a tender abdominal mass.² Almost a litre of bile was drained percutaneously with some short-lived relief of symptoms.

Such classical choledochal cysts are but one form of a range of choledochal malformations, all commoner in females (~4:1), which remain relatively rare in the West compared to China and Japan although real statistics on prevalence do not exist.^{3–5}

Classification

The classification of choledochal malformation is largely morphological and has evolved from a literature review by Alonso-Lej *et al.*,⁶ who separated choledochal cysts into three types (where most classical cystic dilatations of the common bile duct [CBD] were Type 1; the rare diverticulum of the CBD – Type 2 and a distinct distal dilatation of the CBD within the duodenal wall [or choledochocoele] – Type 3). The Japanese

surgeon, Takuji Todani added the concept of a more cylindrical or spindle-shaped extrahepatic dilatation (herein referred to as a 'fusiform' dilatation) in 1985⁷ and introduced the concept of intrahepatic dilatation. Later additions trying to impose the possibly distinct concept of pancreaticobiliary malunion⁸ have also been suggested but have not really been widely adopted by the surgical community.

Our own concept of classification retains the structure of the original (Types 1–5) but, to avoid the semantically difficult 'cystic choledochal cyst' or 'fusiform choledochal cyst' (which is not actually cystic), utilizes the non-judgemental 'choledochal malformation' with whatever descriptive epithet best suits the nature of the dilatation. Thus Type 1c refers to a classical cystic malformation while Type 1f describes a more fusiform appearance (Fig. 1). Caroli's disease (*i.e.* multiple segmental intrahepatic biliary dilatations, and together with congenital liver fibrosis known as Caroli syndrome) is still nominally a Type 5 malformation. However, it should always remain fairly distinct as it is probably: (i) genetic in origin with a resultant biliary ductal plate malformation; and (ii) has a marked association with both cystic renal disease and liver fibrosis,⁹ not seen in any other type.¹⁰

Common types of choledochal malformation

Type 1c

Cystic dilatation of the CBD is the commonest type overall.⁴ Typically, there is a sharp demarcation between the cyst and distal CBD lying behind head of pancreas, which then runs into a common pancreatobiliary channel (> 90%). Unless obstructed, the proximal common hepatic duct (CHD) and gallbladder are relatively normal. In those with long-standing obstruction, there tends to be a stenosis at the level of the common hepatic duct, which presumably protects the more proximal ducts from the elevated intrabiliary pressure (Fig. 2).

Type 1f

Fusiform dilatation of the extrahepatic biliary tree is a more diffuse lesion without such clear distal demarcation and is never as large as the Type 1c. The actual biliary dilatation itself may be subtle and probably merges into a condition sometimes termed forme fruste choledochal cyst or common channel syndrome.¹¹ Again, this is poor terminology but describes a 'normal' biliary tree in association with a

definite (and usually symptomatic) common channel. Whenever the bile ducts are resected in this latter condition, they almost invariably show epithelial denudation and damage (up to 50% in one series).¹¹ Again, > 90% of Type 1f malformations have a demonstrable common channel.

Type 4

Dilatation of both the extra- and intrahepatic parts of the biliary tree is seen in up to 20% of some series.¹¹ One can draw a distinction between those with intrahepatic duct dilatation due simply to an obstructed extrahepatic duct or actual hilar stricture (which returns to normal dimensions after corrective surgery) and those with genuine intrinsic dilated segments. There is, perhaps, an age-related element in these lesions, as discrete intrahepatic dilatation is uncommonly seen in infants and those detected antenatally. This suggests that obstruction, and perhaps sepsis and stone formation, can influence later biliary morphology. Previous classifications referring to a 'Type IVb' with two separate cystic dilatations of the extrahepatic biliary tree almost always seemed to refer to additional dilatation of the common channel – this could probably be discarded.

Aetiology

The aetiology of choledochal malformation is unclear with no real consensus. Competing theories would seem to fall into two groups: (i) those suggesting a true congenital dilatation possibly secondary to an obstructive stenotic segment of the CBD;^{5,12} and (ii) those where there is an acquired bile duct dilatation secondary to reflux of a destructive broth of digestive pancreatic secretions via a

Figure 2 Operative cholangiogram of Type 1c malformation, with clear demarcation at level of CHD and distal CBD; note relatively undilated gallbladder.

Figure 3 Cholangiogram (PTC) of Type 1f (note smooth gradation between normal and abnormal biliary tree) together with dilated common channel filled with radiolucent debris. A patent accessory duct is also visible.

common channel, with secondary mural degradation and dilatation (the Babbitt hypothesis).^{11,15} Evidence both for and against has been mostly inconclusive although certain observations may be pertinent. It is possible to detect choledochal malformations *in utero* using maternal ultrasonography and all of these turn out to be Type 1c malformations.¹⁴ It is possible to measure amylase in bile (obtained at the time of corrective surgery), as a surrogate for degree of pancreatic reflux.¹⁵ In such infants and children, there is a positive correlation with age, probably because the infantile pancreas does not have the capacity to produce amylase; therefore, by implication, any such reflux this early would be devoid of destructive proteolytic enzymes and yet they do have cysts.

Abnormalities of the pancreaticobiliary junction (Fig. 3) are an intrinsic part of the choledochal malformation complex typically consisting of a long common pancreatobiliary channel, an abnormal angle of insertion of the common bile duct, and a variable degree of proximal bile duct stenosis.⁸ They are seen in Type 1c, Type 1f and Type 4 malformations and, of course, are the main abnormality in Type 3 lesions. Wong and Lister¹⁶ showed that the pancreatobiliary ductal junction in early fetal life invariably lies outside the duodenal wall and sphincter muscle complex. By the time of birth, however, the union comes to lie within the wall and the choledochal sphincter; it is failure of this final phase that leads to what we see as an anatomical common channel. Therefore, whether such malunion is simply an expression of disordered more proximal biliary development (and incidental), or is the actual cause of later biliary pathology is a moot point.

We have measured intracholedochal pressure in a series of children coming to surgery.⁵ This showed that the higher pressures were found in those with the lowest bile amylase levels, suggesting that those where the pathology is primarily a segmental CBD obstruction, refluxed less. Those with no obstructive element were free refluxers. Interestingly, there was no relationship of pressure to morphology, although those with the higher pressures were seen in the older children and adolescents.

Clinical features

Symptoms depend largely on the age at presentation. Obstructive jaundice is the main presenting symptom in children whilst abdominal pain is perhaps the commonest feature in adults. Acute symptoms suggest the presence of complications such as cholangitis, pancreatitis or perforation. The classical triad of pain, jaundice and a palpable mass is uncommon occurring in no more than 6% in one UK series.¹⁷ A *de novo* presentation with carcinoma is uncommon but is certainly a feature in adult series (*vide infra*).

Choledochal morphology may favour some features over others. Fusiform lesions are never large enough to be palpable while multiple intrahepatic Type 4 lesions predispose to stone formation and sepsis.

Current approach to diagnosis

A wide variety of imaging techniques are available which will, non-invasively, reconstruct biliary anatomy and give an excellent idea of biliary function. Most lesions are detected by abnormal ultrasonography which should allow precise measurement of the CBD, degree of intrahepatic biliary dilatation and the presence of stones. 3-Dimensional reconstructed magnetic resonance imaging (MRI; Fig. 2) has replaced CT scanning and ERCP as the key anatomical investigation. More so, since the introduction of newer techniques such as non-breath-holding and respiratory-triggered MRI.¹⁸ This can delineate, precisely, the morphology of the choledochal malformation and its relationship with adjacent structures. Non-invasive imaging of the common channel is still difficult for both MRCP (and endoscopic ultrasound,¹⁹ where available) and achieved in only up to 80% of cases in adults,²⁰ and much less in children. Abnormalities in liver biochemistry and coagulation studies might suggest secondary liver impairment but if there are concerns over the degree of injury then a radio-isotope scan (^{99m}Tc-DISIDA) will show baseline liver function and impairment of biliary excretion (it can also be useful in the acute situation if perforation is suspected). Diagnostic ERCP is currently reserved for situations where the degree of biliary dilatation is mild or minimal, or the nature of the pancreatobiliary junction and common channel cannot be determined by MRI alone.

Management

Most choledochal malformations will come to surgical reconstruction. Some centres in South American and Asia have reported ERCP and sphincterotomy alone as definitive treatment for mild fusiform dilatation (or at least a common channel) although their long-term prognosis is not known, given that it does not abolish the pancreatic reflux.²¹

Open surgery dates from 1895 when William Swain first described drainage of a choledochal cyst into an adjacent loop of jejunum.²² Indeed, relatively simple internal drainage procedures (*e.g.* cystoduodenostomy) became the norm during the 20th century, only being replaced by complete excision of the dilated extrahepatic malformation and biliary reconstruction in the last 25 years. Those procedures, which left the cyst *in situ*, when followed up for long enough were plagued by complications such as cholangitis, stone formation (sump syndrome) and, ultimately, malignant change or cirrhosis.^{23,24} Japanese surgeons led the change in surgical philosophy, advocating a much more aggressive approach to biliary excision and reconstruction.⁵ While no one now doubts the wisdom of cyst excision, there has still been controversy about the type of reconstruction. Thus, whether to mobilise a long (≥ 40 cm) jejunal Roux loop and perform a wide hepaticojejunostomy or to mobilise the duodenum and create a hepaticoduodenostomy (favoured by Todani²⁵) has been often debated. The former approach has been favoured by the majority of surgeons in the West and there is now clear evidence that it is indeed associated with better long-term outcomes by minimising late anastomotic complications including stricture.²⁶ What has also become clear is that during open surgery thought should be given to what is being left behind – so the opportunity for a thorough on-table intrahepatic choledochoscopy, *etc.* should not be missed. Strictures can be dilated, stones can be removed and mucosal irregularities can be biopsied.²⁷ A similar proactive approach should be adopted for the common channel, which should be scoped (if possible) and cleaned of occluding debris or stones. Occasionally, a transduodenal sphincteroplasty may be warranted if there is ampullary stenosis and a dilated channel.

All this can, of course, be replicated laparoscopically in both adults and children with perhaps some advantages, particularly in adults of a shorter hospital stay and earlier return to work. Techniques using four or five ports and an extra-abdominal intestinal anastomosis have been described.²⁸ Nonetheless, operative times are long (> 12 h) and this is likely to remain an option in relatively few centres.

Complications

The operative mortality rate, even in comparatively recent series is still significant at $\sim 3\%$,²⁹ and complications can be

seen in 15–20% of patients.^{3,4} These include wound infection, anastomotic bile leak or stenosis, cholangitis and bowel perforation. Complications tend to be lower in children coming to operation earlier. Intrahepatic stone formation (estimated to occur in up to 5% of cases at follow-up) tends to occur with Type V lesions, older children and adults and in those with stones at the original surgery.⁴ Cirrhosis (unless evident at the original surgery) is rare when good bile flow is re-established. Recurrent pancreatitis is certainly a problem, and can manifest many years after the original cyst has been removed. It is related to the still-present common channel and, occasionally, the residual distal CBD which might act as a nidus for stone formation. What is not clear, however, is the risk of malignancy in residual biliary epithelium and this will be addressed separately.

Risk of malignancy in choledochal malformation

Biliary tract cancer is rare in the general population, with an incidence of < 3 per 100,000 population (including gallbladder, intra- and extrahepatic ducts).³⁰ Kasai *et al.*³¹ first noted an apparent association of choledochal malformation with malignancy in 1970, but it remains unknown what proportion of biliary cancers arise in cysts. Watanabe *et al.*³² reviewed data from 73 Japanese institutions in 1987 and identified 154 cases of malignancy from 881 collected choledochal cysts (*i.e.* an incidence of malignant change of 17%).

The bile duct is composed of a fibrous tissue with occasional elastic fibres, lined by a mucosa consisting of a lamina propria and a single layer of tall columnar epithelium with few scattered mucus-producing goblet cells in the distal CBD. The epithelium in choledochal malformations, subject to increased biliary pressure, refluxed proteolytic enzymes and perhaps sepsis, changes – initially showing reactive hyperplasia but later tends to vanish leaving islands of abnormal mucosa in a denuded chronically inflamed fibrous wall. Dysplasia and overt malignancy are age-related features with the youngest patient so far reported a 12-year-old girl with a large cystic malformation who, at presentation, had an invasive, inoperable adenocarcinoma of the distal duct.³³

A number of different histological types have been reported; most are adenocarcinomas of the bile ducts or gallbladder, although squamous carcinoma (presumably arising in an area of squamous metaplasia) is also possible. Rarities included carcinoma arising in a villous adenoma³⁴ and cancer of the distal duct within the pancreas.³⁵ Most cancer arises in the cyst itself (50%) or in the gallbladder (46%) and only small percentage in the intrahepatic ducts ($\sim 2\%$); reflecting the gender disparity, most are in females. The presence of a choledochal malformation changes the time of onset of bile duct malignancy, thus the usual age at onset is in the 3rd decade, 10–20 years sooner than bile duct cancer without cyst (Table 1).

Table 1 Incidence of malignancy in recent series of choledochal malformation

Study	Year	Cases (n)	Rate of malignancy n (%)	Age (range) of presentation (years)
Todani <i>et al.</i> ³⁶	1987	82	8 (10)	–
Chijiwa & Koga ³⁷	1993	46	4 (9)	61 (42–71)
Lipsett <i>et al.</i> ³⁸	1994	42	3 (10)	Adults
Lenriot <i>et al.</i> ³⁹	1998	42	5 (12)	39 (29–51)
Bismuth & Kissat ⁴⁰	1999	48	6 (13)	39 (17–57)
Jan <i>et al.</i> ⁴¹	2000	80	8 (10)	50 (32–81)
De Vries <i>et al.</i> ⁴²	2000	42	6 (14)	36 (20–62)
Visser <i>et al.</i> ¹⁰	2004	39	8 (21)	52 (33–73)

What causes this propensity to malignant change? A number of possibilities have been suggested. Long-standing pancreatic reflux of activated potent pancreatic enzymes such as phospholipase A₂, trypsin and elastase 1, causing ulceration and increased epithelial turnover seems an attractive hypothesis. Similarly, recurrent cholangitis or the irritant effect of biliary tract stones might contribute although the time-scale of this can only be less. Patients with common channel alone have a higher risk of developing biliary tract malignancies (typically gallbladder adenocarcinoma) than the general population and often do not have stones or cholangitis,⁴⁵ suggesting that the former is more likely. The prevalence of carcinoma of the gallbladder in APBD varies according to the population endoscoped; however, one recent Japanese prospective ERCP study found an incidence of ~11% in adults with common channel.⁴⁴

Why the concern? Well, the prognosis of biliary malignancy is appalling because of early extensive local and regional spread at presentation; as a consequence, the 5-year survival even for those who undergo surgery is < 40% and close to zero for the remainder.⁴⁵

What then for adult patients from a different era with, in retrospect, inadequate surgery? In the fit patient, even if currently asymptomatic, the answer really should be to aim for revisional surgery with resection of all the extrahepatic at-risk mucosa. There are no reliable methods of diagnosing mucosal dysplasia and malignant change short of open biopsy; once malignancy has developed, prospects of cure by surgery and adjuvant therapy are poor. Some cysts may have a residual connection to the duodenum and perhaps ERCP and intracystic brush cytology might have some role, although this seems unlikely.

It is not really known whether current definitive excisional surgery with Roux-en-Y reconstruction will reduce the risk of malignancy in the intrahepatic biliary mucosa left *in situ*. This so-called ‘stump’ cancer has been reported but caveats are usually added. Thus, Yamamoto *et al.*⁴⁶

reported a 60-year-old women with anastomotic adenocarcinoma following earlier hepaticojejunostomy and excision of a choledochal dilatation. However, this had only been 5 years earlier. There are a small number of other similar cases³² and also some where the malignancy arose in the distal retained bile duct within the pancreas.³⁵ Fortunately, it appears that no child < 10 years of age having excisional surgery as described above has developed later malignancy – but only time will tell. The low proportion of malignant change in the liver (< 2%, as compared to the cyst or gallbladder) in untouched choledochal malformations is a cause for optimism certainly.

Follow-up and transitional care

Children treated according to today's standards still require, we believe, life-long follow-up. Mostly this will be in the hands of others, not involved in the original surgery. In the first 10 years, the absolute minimum should be to demonstrate restoration of normal bile flow. Any suggestion of recurrent cholangitis or intrahepatic biliary dilatation warrants functional evaluation of the anastomosis using radioisotopes and/or percutaneous cholangiography. Into adulthood, the real problem will be in trying to detect malignant change in residual biliary epithelium and that with today's imaging is difficult. Regular, annual or bi-annual, liver ultrasonography appears to be a sensible first step to establish the principle of follow-up, possibly with the addition of biochemical markers of liver function. Whether the addition of regular MRCP or putative tumour markers improves the quality of surveillance, however, is not known.

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