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Biliary cystic disease and neoplasia: surgical management

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Background

Congenital cystic dilatation of the extra- and intrahepatic bile ducts is a rare condition with several potential complications, especially a high risk of malignant degeneration, which may develop from an anomalous arrangement of the pancreatico-biliary ductal junction.

Patients

Twenty-two patients with cystic dilatation of the biliary tree, subdivided according to the Todani classification, were observed and treated during a 17-year period. The intrahepatic ducts were involved in 15 patients.

Results

Surgical treatment involved either total excision of extrahepatic cysts, hepatic resection in cases of segmental intrahepatic disease or, in the presence of diffuse intrahepatic disease, a wide biliary–digestive anastomosis performed onto the biliary confluence, with the intent of reducing the risk of neoplastic degeneration. One patient with extensive and symptomatic liver involvement complicated by biliary cirrhosis has already undergone liver transplantation, and another two patients who are currently asymptomatic may require this procedure in future. Neoplastic degeneration was found in three patients (one each of Todani type I, type IVa and type V), or 14% of the series. The postoperative course was complicated by cholangitis in only two patients, who were treated successfully with antibiotics. Except for one patient with a type I cyst complicated by carcinoma, who died 14 months post-operatively, all patients are alive and well at a mean follow-up of eight years (range 8 months to 17 years).

Discussion

The ideal surgical procedures to cure the disease and prevent malignant degeneration are: (a) complete excision of the extrahepatic biliary cysts; (b) hepatic resection in cases of segmental intrahepatic involvement; (c) wide bilio-digestive anastomosis in cases of multiple intrahepatic involvement, or liver transplantation when this is complicated by secondary biliary cirrhosis.

Keywords

choledochal cyst, bile duct resection, cholangiocarcinoma.

Introduction

Biliary cystic disease, which is very widespread in the Orient but rare in Western countries, represents an important chapter in biliary pathology due to the possibility of malignant degeneration [1–10]. There are numerous hypotheses regarding its pathogenesis. Among the more plausible, Yotsuyanagi correlates the malformation with partial atresia of the distal common bile duct and consequent proximal dilatation [11]. According to Babbitt *et al.*, the cystic ectasia arise from an anomaly at the biliopancreatic confluence, which allows pancreatic juice to reflux into the distal bile duct causing chronic inflammation and fibrosis [12]. Alternatively, Kusunoki *et al.* have suggested that the narrowing of the distal duct is due to a lack of postganglionic cholinergic activity, with subsequent cystic dilatation above this segment [13]. Different malformations may occur simultaneously at different levels with or without an element of biliary atresia, lending support to the idea that these lesions represent various manifestations of a single pathological process [14].

The frequent association of an intrahepatic malformation with extrahepatic biliary cysts should not be considered a chance occurrence. It is therefore generally believed that Caroli's disease is part of the wide spectrum of extrahepatic biliary cystic dilatation [15]. Recognising a common congenital origin, Todani *et al.* [16] broadened the

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Alonso-Ley classification, which described only three types of cysts [17], by adding two new forms: type IV, a and b, and type V (Caroli's disease). According to Desmet [18], Caroli's disease belongs to the wide spectrum of malformations that results from remodelling of the ductal plate, which is the embryological structure from which bile ducts derive.

Cystic dilatation of the biliary tract has a strong predisposition for the female sex (67–86%). Although it is a congenital disease, it is not discovered until adulthood in 25% of the patients. The late appearance of clinical disease could reflect a less severe malformation, which might remain unrecognised for many years. The usual symptoms are epigastric and right hypochondrial pain, jaundice, recurrent cholangitis and a palpable abdominal mass. The routine use of ultrasound and spiral computed tomography (CT) scans plus either percutaneous transhepatic cholangiography (PTC) or endoscopic retrograde cholangio-pancreatography (ERCP) allows classification of the type of lesion and preoperative planning for the correct surgical strategy. There is a high risk of malignant degeneration: 2.5–28% in extrahepatic cysts, 7–14% in intrahepatic cysts and 50% in patients with a previous cystenterostomy. This fact influences surgical treatment by making complete excision preferable to the simpler procedure of cyst drainage [2–5].

The present paper reports a personal series of 22 patients over an 18-year period and highlights the presentation and management of biliary cystic disease.

Patients and methods

Since 1981 we have observed 22 patients with biliary cystic disease: 18 females (82%) and 4 males (18%), with a median age of 38 years at the time of diagnosis (range 6 –72 years). The predominant symptom on admission was epigastric and right hypochondrial pain, which was accompained by jaundice and fever in 90% of cases. Only four patients (18%) presented with the classical triad of pain, jaundice and a palpable abdominal mass; in two of these the mass was due to hydrops (mucocele) of the gallbladder.

Laboratory values on admission included elevated levels of direct bilirubin (median value 21.3 μmol L^{-1}), alkaline phosphatase, γ-glutamyl-transferase (in 12 patients), and transaminases (in 9 patients). A preoperative diagnostic algorithm utilising ultrasound scan, spiral CT scan, PTC and/or ERCP, allowed classification of disease into the following types (Figure 1):

Type I: seven patients (32%).

Type IVa: seven patients (32%), three with diffuse involvement of the right posterolateral segments, two with segmental localisation to the left hepatic lobe and two with an extensive bilateral distribution of intrahepatic cysts.

Type V: eight patients (36%), four with intrahepatic localisation to the left liver, three with multiple bilateral involvement and one with multiple cysts in the posterolateral segments of the right liver.

Results

Operative treatment (Table 1)

The seven patients with type I cysts were treated by total excision of the extrahepatic cyst and reconstruction with a wide biliary–enteric anastomosis (Roux-en-Y) at the biliary confluence.

Five of the seven patients with type IVa cysts, given the low incidence of neoplastic degeneration within the liver, were also treated by resection of the extrahepatic cyst alone. In the two patients with segmental localisation of the cysts to the left liver, a left lobectomy was performed in one case and a left hepatectomy in the other. The reconstruction was performed by means of hepatico-jejunostomy Roux-en-Y in five patients and by means of a short isolated jejunal loop anastomised proximally to the biliary tree and distally to the duodenum (hepatico-jejuno-duodenoplasty) in the other two.

In the group of eight patients with type V cysts, hepatic resection was performed in four (one left lobectomy, three left hepatectomies). One of the hepatectomies was extended to the right to include segments V and VI and another was extended to the caudate lobe due to carcinoma within the cyst extending along the duct towards the confluence. The fifth patient, a six-year-old boy with multiple intrahepatic cysts in the posterior segments, was treated with a wide biliodigestive anastomosis at the hepatic hilus. Of the remaining three patients with multiple diffuse bilateral intrahepatic cysts complicated by biliary cirrhosis, two are candidates for liver transplantation while one already received a transplant one year ago after 22 years of recurrent cholangitis.

Outcome

There were no in-hospital deaths following operation. The results of the different surgical procedures were as follows.

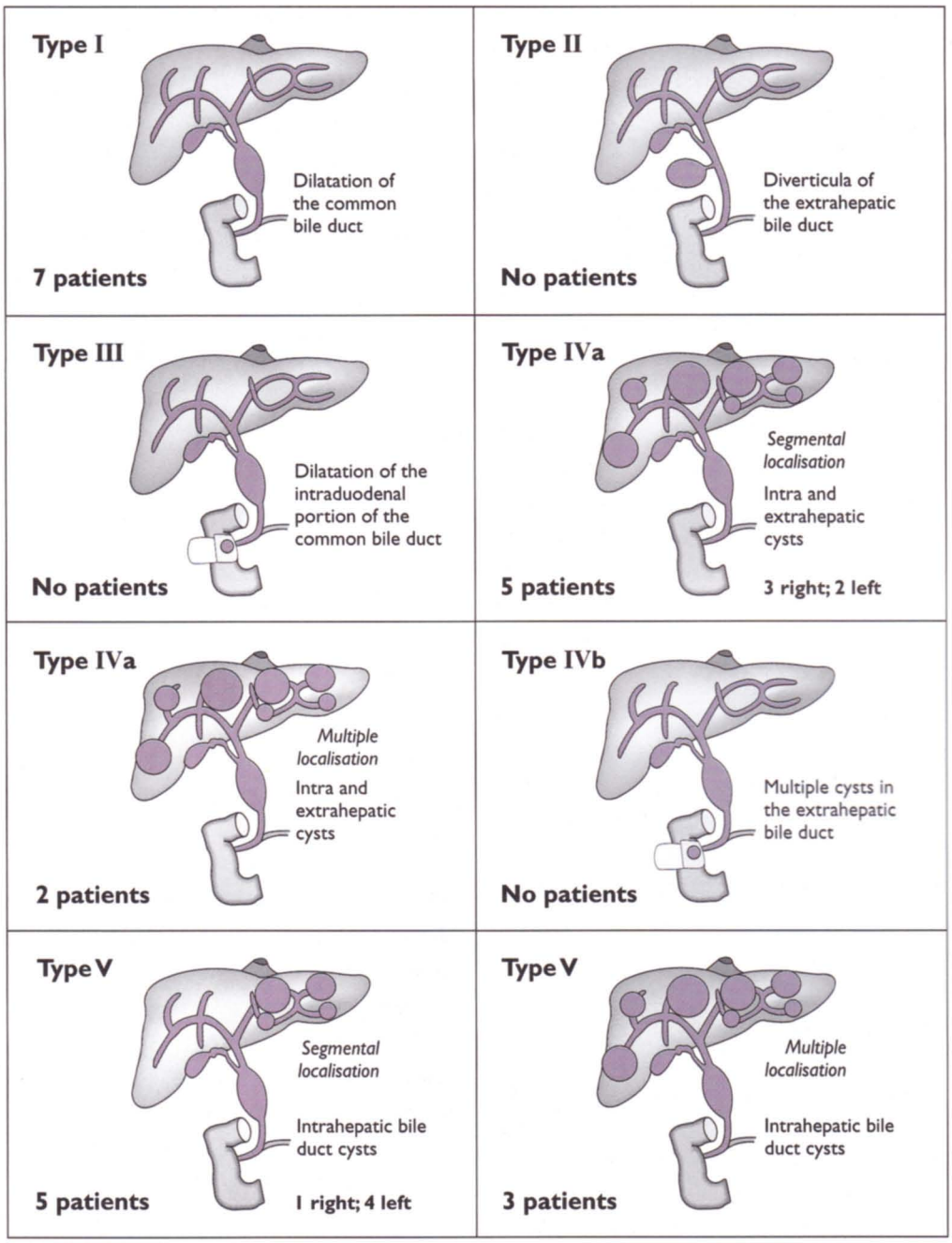

Figure 1. *Todani classification adapted to our series, and numbers of patients for each type.*

Type I cysts

The postoperative course was uneventful in six patients (mean hospital stay 12 days; range 10–24 days) but was complicated by wound infection in the seventh patient (postoperative hospital stay 29 days). Follow-up for a mean eight years (range 1–17 years) demonstrated good clinical and laboratory results in five patients. One patient had cholangitis one month after operation and required antibiotic treatment. In the oldest patient in this group, definitive histological examination of the specimen revealed moderately differentiated adenocarcinoma infiltrating the posterior wall of the cyst but without involvement of the resection margins (Figure 2). This patient died 14 months later from diffuse hepatic metastasis.

Type IVa cysts

The postoperative course was uncomplicated in all seven patients, with a mean hospital stay of 15 days (range

Table 1. *Choledochal cysts in 22 patients: type of lesion, surgical treatment and malignant degeneration*

Type	Cases (%)	Surgical treatment	(n)	Malignant degeneration (n)***
Type I	7 (32%)	Resection of extrahepatic cysts	(7)	Extrahepatic cyst (1)
Type IVa	7 (32%)	*Resection of extrahepatic cysts	(5)	
		**Resection of extrahepatic cyst+left lobectomy	(1)	Extrahepatic cyst (previous cystenterostomy) (1)
		***Resection of extrahepatic cyst+left hepatectomy	(1)	
Type V	8 (36%)	**Left lobectomy	(1)	
		**Left hepatectomy	(1)	
		*Left hepatectomy extended to V–VI segments	(1)	
		**Left hepatectomy extended to caudate lobe	(1)	Left intrahepatic cyst (1)
		*Bilio-digestive anastomosis	(1)	
		*Liver transplantation	(1)	
		*Candidates for liver transplantation	(2)	

* Multiple sites in the right liver or bilateral involvement by intrahepatic cysts

** Segmental localization of intrahepatic cysts

*** 14%

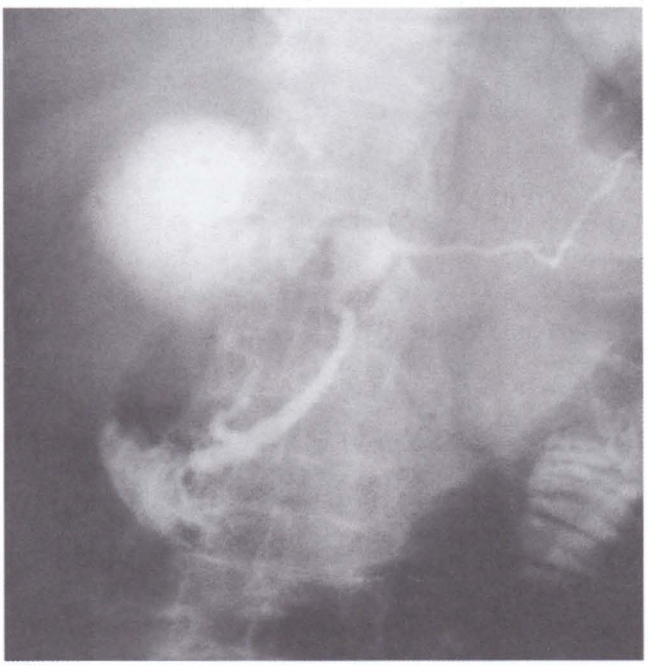

Figure 2. *Type I cyst with malignant degeneration. ERCP showing an anomalous pancreatobiliary ductal connection, with a long common channel (> 15 mm).*

12–31 days). Follow-up for a mean 10 years (range 1–17 years) revealed a good clinical and biochemical result in six cases. One patient only had episodes of cholangitis one month postoperatively and was successfully treated with antibiotics. One patient who had been treated 19 years earlier by means of cystenterostomy underwent total excision of the extrahepatic cyst plus left hepatectomy; histological examination showed a well-differentiated adenocarcinoma infiltrating the left posterior wall of the extrahepatic cyst, but the resection margins were free of tumour (Figure 3).

Type V cysts

The postoperative course in five of the six operated patients was satisfactory with a mean hospital stay of 16 days (range 10–29 days). One patient with left hepatectomy extended to segments V and VI developed a subphrenic abscess and required reoperation for drainage and subsequent targeted antibiotic therapy for *Acinetobacter* sp. with a total hospital stay of 73 days. Follow-up for a mean eight years (range 8 months to 16 years) demonstrated good clinical and laboratory results in all operated patients. In particular the patient with a moderately differentiated adenocarcinoma of the left intrahepatic cyst that spread to the confluence is alive at two years, while the 24-year-old woman treated with liver transplantation is well one year later (Figure 4).

Discussion

In the past, the diagnosis of cystic dilatation of the biliary tree was nearly always an incidental finding at the time of operation. Surgical treatment consisted of simple cystenterostomy or partial resection in the case of extrahepatic cysts, while disease with intrahepatic involvement was not taken into consideration. Although associated with a relatively low mortality rate, these procedures resulted in a high incidence of postoperative complications including stenosis of the bilio-digestive anastomosis, recurrent

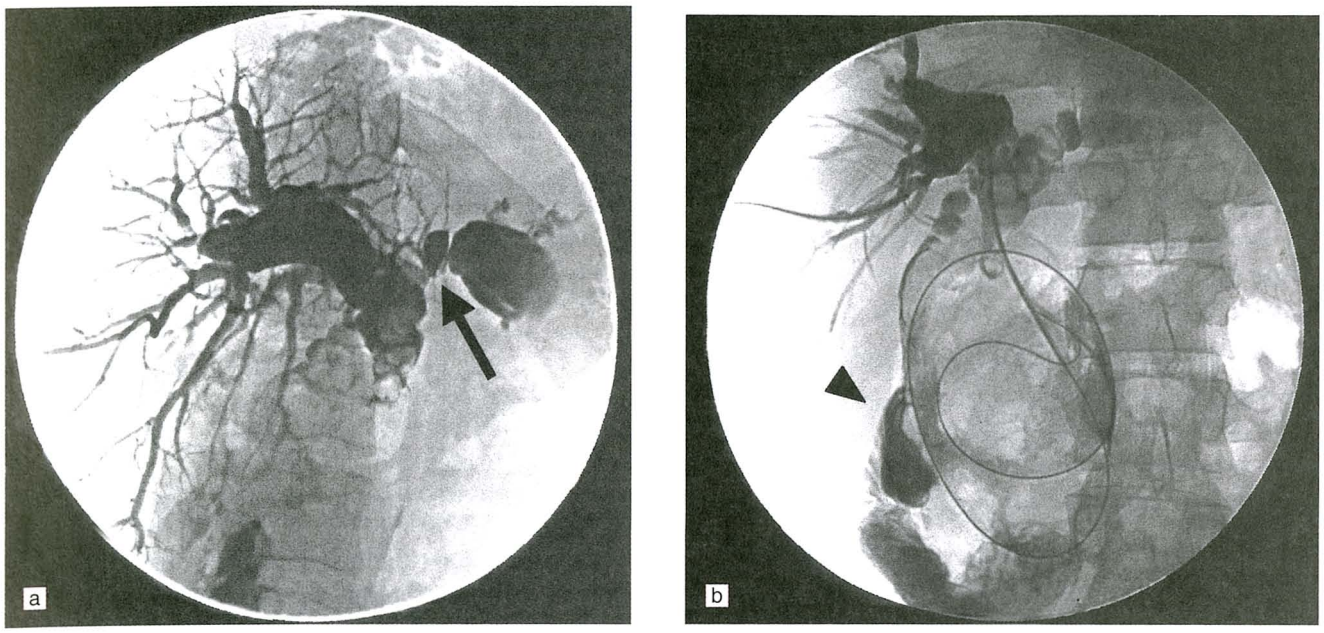

Figure 3. *Type IVa cyst with malignant degeneration. Percutaneous transhepatic cholangiograms showing (a) left hepatic duct stricture (arrow) and cystic dilatation of proximal left biliary tree and (b) huge extrahepatic choledochal cyst lined by the loop of the guidewire. The anastomosis site of the previous cystenterostomy is shown (arrowhead).*

cholangitis, lithiasis and possible carcinomatous degeneration of the drained cyst, as illustrated by one of our type IVa cases [2,4,6].

Nowadays, it is possible to obtain a preoperative diagnosis in all patients by using a diagnostic protocol that comprises ultrasonography, spiral CT scan, PTC or ERCP and hepato-biliary scintigraphy. Accurate preoperative diagnosis and determination of the precise intrahepatic localisation (whether segmental or diffuse) are important factors in establishing the correct surgical strategy.

The possibility of neoplastic degeneration of the cyst must be carefully considered. There were three such patients in our series, or 14% of the total group: one intrahepatic and two extrahepatic. Extrahepatic cysts are at particular risk of cholangiocarcinoma. In Japan the presence of biliary neoplasia is 1000–2000 times higher in patients with choledochal cyst than in the general population [19].

An anomalous pancreaticobiliary–ductal union has been reported in 90% of patients with cystic dilatation of the bile duct and is relevant to cholangiocarcinoma development because of the degenerative changes that follow reflux of pancreatic juice, cholestasis and repeated bacterial infection as well as possible mutation of the c-Ki-*ras* gene at codon 12 in the DNA of biliary epithelium [19–22]. In a review of 106 cases of bilio-pancreatic neoplasia occurring in association with cystic dilatation (with or without previous operation), the neoplasm was limited to the cyst in only 31%; in the other 69% it arose elsewhere in the biliary tract, in the gallbladder or in the pancreas [7]. It follows that to prevent malignant degeneration in patients with an anomalous ductal junction, extrahepatic disease must be treated by complete excision of the cystic malformation as soon as possible after diagnosis.

In patients with intrahepatic cysts the solution must be varied. If the disease is confined to one half of the liver the ideal procedure is hepatic resection [23–25], but the need

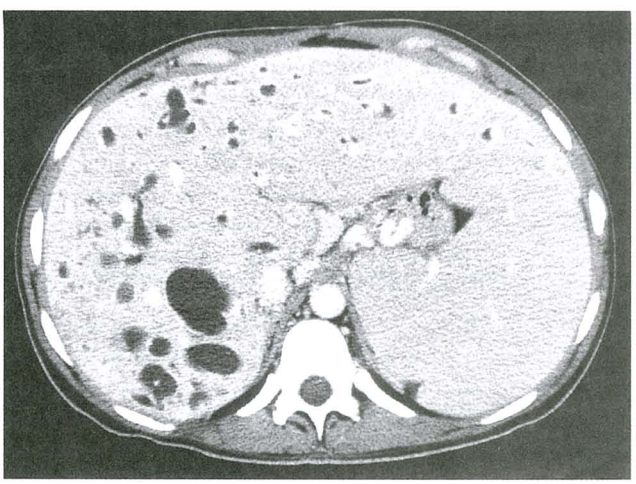

Figure 4. *Type V cyst. Contrast-enhanced CT scan showing multiple intrahepatic biliary cysts with peripheral thin rim enhancement, indicating superimposed cholangitis, and splenomegaly secondary to biliary cirrhosis.*

for a wide hepatectomy for intrahepatic cysts must be weighed against the lower risk of malignancy at this site. We believe that when the cysts are at multiple intrahepatic sites, a wide bilio-enteric anastomosis can be considered a valid therapeutic approach since it resolves the problems of bile stasis and consequent lithiasis, which are probably the initiating factors in malignant degeneration [26–29]. There are only eight cases in the literature in which patients with type I or type IVa cysts have developed intrahepatic neoplasia following resection of the extrahepatic cyst [20].

In general, resection is feasible for cysts of the left liver, while cysts of the right liver are more demanding, especially when they are diffuse. We prefer to avoid right hepatectomy unless absolutely indicated. In patients with multisegmental Caroli's disease complicated by secondary biliary cirrhosis, liver transplant represents the only therapeutic possibility.

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