Original Article

Choledochal cysts with malignancy in adult: A retrospective study with an experience of twenty-two years

Ji-Feng Feng[1], Wen-You Chen[2], Da-Feng Chen[3], Song Zhou[4], Jing Liu[5]

ABSTRACT

Objective: To study the diagnosis, therapy, precaution, and prognosis after surgical treatments of malignant changes that occurred in adult choledochal cysts.

Methodology: We analysed retrospectively the clinicopathologic data, the ways of operative treatment and the survival time of patients with malignancy in 74 cases of adult choledochal cysts in our hospital from 1986 to 2008.

Results: Among the 74 patients, 9 cases (3 males and 6 females) had carcinomas arising from choledochal cysts at the mean age of 51.6 ± 16.4 years (range: 22 to 72 years) with the prevalence of 12.2% (9/74), which was significant difference comparing with no malignant change groups (P=0.0037). The prevalence of malignancy for different groups were closely related to the age increased (r=0.363, p=0.011): 3.4% for 16-30 group (1/29), 8.7% for 31-45 group (2/23), 15.4% for 46-60 group (2/13), and 44.4% for 61-75 group (4/9), respectively. Surgical treatments included cysts excision with Roux-en-Y hepaticojejunostomy in three patients, cysts excision with cholangiojejunostomy in two patients, partial cyst excision with left lobectomy and Roux-en-Y hepaticojejunostomy, pancreatoduodenectomy, chemotherapy with implantable drug delivery system via hepatic artery and portal vein, and choledochotomy with T-tube drainage and metastatic lymph node biopsy in one patient, respectively. The survival time was from three months to 66 months with the mean survival of 19.1±18.6 months.

Conclusion: Choledochal cyst is a premalignant lesion, and the incidence of malignancy increases remarkably with the increase in age. Patients require close monitoring so that recurrent carcinoma of the remnant bile duct can be identified as early as possible.

KEY WORDS: Choledochal cyst, Bile duct, Carcinoma, Malignant change, Malignancy.

Pak J Med Sci January - March 2011 Vol. 27 No. 1 6-10

How to cite this article:

Feng JF, Chen WY, Chen DF, Zhou S, Liu J. Choledochal cysts with malignancy in adult: A retrospective study with an experience of twenty-two years. Pak J Med Sci 2011;27(1):6-10

INTRODUCTION

Choledochal cyst is dilatation of the extrahepatic, intrahepatic biliary tree or both, which usually manifests in the paediatric age group.[1,2] Choledochal cyst is a rare congenital condition with a high risk of malignancy if untreated, and the incidence of malignant change increases remarkably with the increase in age.[3] Choledochal cyst with malignancy is an extremely rare condition in adult, and the clinical symptom is non-specific, the preoperative diagnosis is difficult, and the prognosis is poor.[4-6]

The purpose of the present study was to determine the clinical course of malignant change of adult choledochal cyst, with emphasis on the diagnosis, therapy, precaution, and prognosis after surgical treatments.

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* Received for Publication: June 16, 2010

* Revision Received: November 6, 2010

* Revision Accepted: November 10, 2010

METHODOLOGY

Clinical material: Patients with choledochal cysts, who were seen at Department of General Surgery,

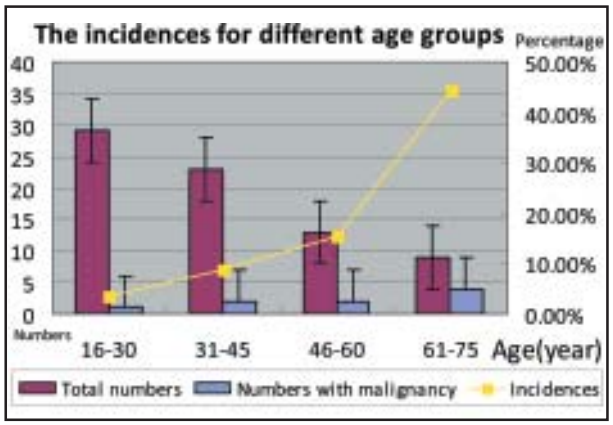

Fig-1: The incidences of malignant change for different groups were closely related to the age increased.

Southeast Hospital affiliated to Xiamen University from 1986 to 2008. We analysed retrospectively the clinicopathologic data, the ways of operations and the survival of patients with malignant changes in 74 cases of adult choledochal cyst.

Statistical analysis: We used t-test, chi-square test, and Pearson's correlation by employing SPSS software version 13.0 for statistical analysis. Quantitative variables are presented as mean ± standard deviation, and qualitative variables as percent. All p values less than 0.05 were considered to be statistically significant.

RESULTS

Nine patients (three males and six females) were proved carcinoma in pathology in all 74 adult choledochal cysts at the mean age of 51.6 ± 16.4 years (range: 22 to 72 years old) with the prevalence of 12.2% (9/74), which was significant difference comparing with no malignant change group with the mean age of 35.9 ± 14.4 years (range: 17 to 74 years old) regarding their ages (P=0.0037) (Table-I). The incidence of malignancy for different groups were closely related to the age increased (r=0.363, p=0.011): 3.4% for 16-30 group (1/29), 8.7% for 31-45 group (2/23), 15.4% for 46-60 group (2/13), and 44.4% for 61-75 group (4/9), respectively (Fig-1). According to Todani's classification, six patients had a type I choledochal cyst (66.7%), and three patients had a type IVa choledochal cyst (33.3%). No patient in the present series had a type II, III, IVb or V choledochal cyst. The duration from cyst to carcinoma was from two months to 20 years (n=8), except one male in which carcinoma in the cystic wall was found during surgery at the first time.

Table-I: Comparison of choledochal cysts with or without malignancy.

	Choledochal cyst with malignancy (n=9)	*Choledochal cyst without malignancy (n=65)*	*P-value*
Gender, n (male/female)	3/6	20/45	>0.05
Age, years (mean±SD)	51.6 ± 16.4	35.9 ± 14.4	0.0037
Todani's type, n			
I	6	46	>0.05
II	0	3	
III	0	1	
IVa	3	15	
IVb	0	0	
V	0	0	

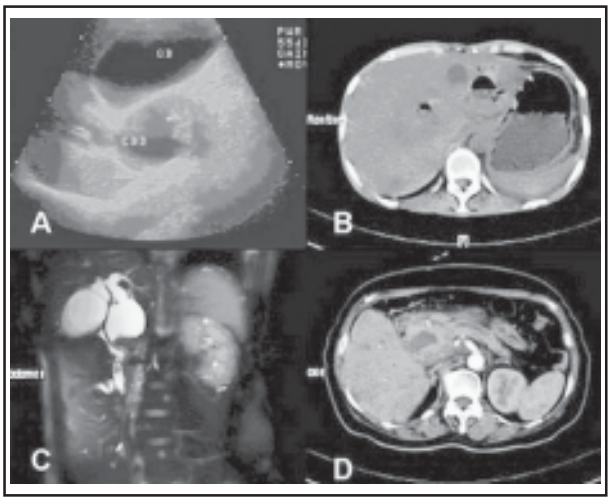

Fig-2: US showed bile duct dilated (Fig-2A), CT showed multiple solid masses in the liver (Fig-2B), MRI revealed bile duct dilated with the filling defects in it (Fig-2C), and the head of pancreas enlarged with the dilated bile duct and pancreatic duct (Fig-2D).

Previous surgery: Only one male had carcinoma in cystic wall found during surgery at the first time, the remaining eight cases had previous surgery for choledochal cyst (88.9%, 8/9). Six out of the 8 patients received previous surgery once, and other two cases received previous surgery twice. The total numbers for previous surgery was 10 times (Table-II).

Table-II: Previous surgery for choledochal cysts.

The type of operation	*n*
Cystoduodenostomy	4
Roux-en-Y cystojejunostomy	3
Cholecystectomy + T-tube drainage	2
Cholecystectomy	1
Total	10

Clinical symptoms: The disease mainly manifested the symptoms of cholangitis, including abdominal pain (100%, 9/9), accompanying with the radiating pain (33.3%, 3/9), jaundice (77.8%, 7/9), fever (55.6%, 5/9), and abdominal mass (22.2%, 2/9).

Imaging examination: Ultrasound (US) was performed in eight cases, five cases showed the dilated bile duct (62.5%, 5/8) (Fig-2A). Computed tomography (CT) was performed in seven cases, six cases showed the dilated bile duct, and one case showed multiple solid masses in the liver (Fig-2B). Magnetic resonance imaging (MRI) was performed in two cases, one case revealed dilated bile duct with the filling defects in it (Fig-2C), and the other revealed the head of pancreas enlarged with the dilated bile duct and pancreatic duct (Fig-2D).

Surgical methods: The types of operations performed for the 9 patients are shown in Table-III.

Surgical complications: Complications occurred in three patients (33.3%, 3/9) (Table-IV).

Site of malignancy: Five patients had carcinoma of the cystic wall (55.6%), three patients had carcinoma of the choledochal duct (33.3%), and one patient had carcinoma of the intrahepatic duct (11.1%).

Pathological results: Pathological results showed adenocarcinoma in six cases (66.7%) (poorly differentiated adenocarcinoma in two cases, moderately differentiated adenocarcinoma in three cases, and well differentiated adenocarcinoma in one case) (Fig-3A), cholangiocellular carcinoma in one case (11.1%) (Fig-3B), cystadenocarcinoma in one case (11.1%), and poorly differentiated squamous cell carcinoma in one case (11.1%), respectively.

Survival: The survival time was from three months to 66 months with the mean survival of 19.1 ± 18.6 months (Table-III).

DISCUSSION

Choledochal cysts are rare cystic dilatations of the intrahepatic or extrahepatic bile ducts, which carry a risk of biliary tract carcinoma.[3,5,7] Voyles et al[8] examined the malignant degeneration that occurred as a long-term complication of a choledochal cyst showing the incidence of carcinoma varies with age at the initial appearance of symptoms. The child with a choledochal cyst that appears before 10 years of age carries a minimum risk (0.7%) of subsequent malignant degeneration compared with the patient in the second decade (6.8%) and older (14.3%). In our study, the prevalence of malignant change was 12.2%. The incidences for different adult groups were closely related to the increase in age: 3.4% for the 16-30 group, 8.7% for the 31-45 group, 15.4% for the 46-60 group, and 44.4% for the 61-75 group, respectively. Based on our finding, we conclude that if someone has an age of over 60 years with previous surgery of choledochal cyst, we should be on a high alert of the possibility of malignant change.

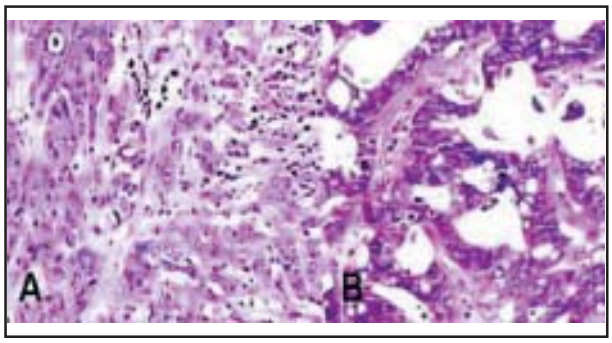

Fig-3: Pathological results showed adenocarcinoma (Fig-3A) and cholangiocellular carcinoma (Fig- 3B).

The etiology of malignant changes of choledochal cysts is unclear, probably as a result of a series of pancreatic juice reflux, chronic inflammation, dysplasia with or without intestinal metaplasia, and invasive carcinoma.[7,9,10] A reflux of pancreatic juice into the biliary tract caused by pancreaticobiliary maljunction has been considered important in the development of malignant change.[9,11] The anatomic variant of a long common channel for the common bile and pancreatic ducts is known to be associated with choledochal cysts. It has been proposed that this

Table-III: Surgery for choledochal cysts with malignancy.

The type of operation	*n*	*Survival*
Cysts excision + Roux-en-Y hepaticojejunostomy	3	17m (alive), 22m (alive), 66m (dead)
Cysts excision + cholangiojejunostomy	2	13m (alive), 19m (dead)
Partial cyst excision + left lobectomy + Roux-en-Y hepaticojejunostomy	1	7m (dead)
Pancreatoduodenectomy	1	16m (alive)
Chemotherapy with implantable drug delivery system	1	3m (dead)
Choledochotomy +T-tube drainage + metastatic lymph node biopsy	1	9m (dead)
Total	9	

Table-IV: Operative complications of choledochal cysts with malignancy.

Complication	*n*	*Treatment*
Early bile leak	2	Percutaneous drainage
Pulmonary infection	1	Anti-infection and anti-inflammatory

anatomic variant promotes reflux of pancreatic juice into the common bile duct, resulting in inflammation, weakening of the bile duct wall, and dilatation.[10] Todani et al[12] reported that patients with previous internal drainage developed cancer at a mean age of 35.6 years, approximately 10 years after cystojejunostomy or cystoduodenostomy. In our series, 8 cases had previous surgery (88.9%). Six out of the eight patients received previous surgery once, and other two cases received previous surgery twice. Therefore, the total numbers for previous surgery was 10 times. Seven patients had previous internal drainage with cystojejunostomy in four cases and cystoduodenostomy in three cases. The duration from cyst to carcinoma was from two months to 20 years. Two cases had duration of 15 and 20 years, respectively. Therefore, it coincided with Todani's study.[12] Patients with a long-term inflammation by reflux of pancreatic juice into the biliary tract caused by pancreaticobiliary maljunction was considered impartment in the development of malignant change.

Early symptoms of choledochal cysts with malignancy are less, and non-specific, so the early diagnosis is difficult. The majority of the cases are accidental discovery during the operation, or even re-operation. The symptoms of cholangitis, including abdominal pain, accompanying with the radiating pain, jaundice, fever, or abdominal mass have no specificity comparing with choledochal cysts.[4,13] With the development of imaging, preoperative diagnosis has increased, US and CT can reveal substantial mass in expanded bile duct, MRI can show filling defects in the expanded bile duct. This group of preoperative US in eight cases, and five cases showed bile duct expanded (62.5%). In our study, US was likely chosen as the initial study based on a presumptive diagnosis. In addition, it must be noted that this study spans 22 years of data collection and includes a time when cross-sectional imaging was used less commonly. CT was performed in 7 cases, 6 cases showed bile duct expanded (85.7%), and one case showed multiple solid masses in the liver (14.3%). MRI was performed in two cases, one case revealed dilated bile duct with the filling defects in it, and the other revealed the head of pancreas enlarged with the dilated bile duct and pancreatic duct. When the diagnosis was unclear on the basis of US or CT, or MRI, imaging of the biliary anatomy with ERCP, MRCP, or percutaneous transhepatic cholangiography was performed.[14,15] Therefore, if the choledochal cyst is papillary accompanying with the imaging characters, we should be on a high alert of this disease. We should also take care of the space occupied lesion in the liver after the operations of choledochal cysts, which is highly suspected as malignancy, especially choledochal cysts in patients with incomplete resection. At all events, we should performed intraoperative frozen sections biopsy in order to diagnose as early as possible.

For the treatment of choledochal cyst with malignancy, the standard surgical method is complete excision of the malignancy together with Roux-en-Y hepaticojejunostomy.[16,17] Hepaticojejunostomy is necessary for patients because complications such as cholangitis, biliary cirrhosis, portal hypertension, lithiasis, rupture and pancreatitis, were frequently encountered in cases of malignant change.[18] In our study, three cases had cysts excision with Roux-en-Y hepaticojejunostomy, one case was dead with the survival of 66 months, the other two cases were still alive with the survival time of 17 and 22 months, respectively. Two cases had cysts excision with cholangiojejunostomy, the survival was worse than patients with hepaticojejunostomy. One case had pancreaticoduodenectomy with the cyst complete excision, also achieved a good result because of the complete excision of the malignancy. One case had metastatic carcinoma in liver who had choledochal cyst 15 years ago. She was admitted to our hospital at the end-stage. The surface of the liver covered with nodules with various sizes, and the cancerous cell spreaded all over the liver and bile duct. Surgical resection was not feasible. So we used chemotherapy with implantable drug delivery system as a conservative therapy. One case had choledochotomy with T-tube drainage and metastatic lymph node biopsy. The result of these two cases were not good. Based on our study of these cases of choledochal cyst with malignancy, the best treatment was cysts excision with Roux-en-Y hepaticojejunostomy. Pancreaticoduodenectomy was also a good treatment because of the complete excision of the malignancy.

CONCLUSION

Reviewing our 22-year experience with choledochal cyst with malignancy, we conclude that choledochal cyst is a premalignant lesion, the incidence of malignancy increases remarkably with

the increase in age. Our study showed that if someone has an age of over 60 years old with previous surgery of choledochal cyst, we should be on a high alert of the possibility of malignant change. In addition, of these cases of choledochal cyst with malignancy, the best treatment was cysts excision with Roux-en-Y hepaticojejunostomy. Pancreaticoduodenectomy was also a good treatment because of the complete excision of the malignancy. In conclusion, patients require close monitoring so that recurrent carcinoma of the remnant bile duct can be identified as early as possible.

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Author Contributions:

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Ji-Feng Feng, Wen-You Chen and Da-Feng Chen analyzed the data,
Ji-Feng Feng and Jing Liu wrote the paper.

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