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Original Article

Cirrhotic Changes in Choledochal Cyst in Relevance to Increasing Age at Presentation

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Abstract

Background: To analyze the relationship between the changes to the liver histology with increasing age in patients with choledochal cyst.

Methods: In this prospective, descriptive study all the patients presenting with choledochal cyst upto 12 years of age were included. The clinical features, liver function tests, ultrasonography, HIDA scan and per operative cholangiogram were selectively done. A total of 53 patients underwent hepatico-jejunostomy. Per-operative liver biopsies were taken in all cases and correlation with age of patient was calculated.

Results: Ultrasound was found to be a reliable investigation in diagnosing choledochal cyst. CT scan was found to be superior as detailed anatomy could be defined. The histological finding that evolved with increasing age was biliary cirrhosis. The incidence of cirrhotic changes was found to be 50% in children of age group 0-2 years and 63% in 2-12 years age group. The correlation was found significant(p-value= 0.015).

Conclusion: Age of the patient with choledochal cyst has significant impact on liver histology. Cirrhosis develops more frequently with increasing age. Early diagnosis and prompt treatment is necessary for a good outcome.

Key Words: Choledochal cyst, Liver biopsy,Liver cirrhosis

Introduction

Choledochal cyst is dilatation of extra hepatic or intrahepatic billiary tree. According to the age of patient at presentation, the effect of cholestasis on liver histology also varies. The increased incidence of cirrhotic and carcinomatous changes is main concern of untreated or late presenting choledochal cysts. There are currently very few studies available to document this aspect. Choledochal cysts (CC) are congenital anomalies of bile ducts which involve dilatations of extra hepatic or intra hepatic billiary tree or both. It is relatively common in Asia and rare in United States and western world. There is a female preponderance with male to female ratio of 1.3 to 4. [1]

Based on analysis of cholangiographic findings the varieties include type I to Type V. The cyst could be due to an anomalous arrangement of the pancreatic or biliary duct system. Clinical presentation of almost all cases with cholestatic disorders is similar namely jaundice, choleuria, hypocholic or acholic stools, hepatomegaly with or without splenomegaly. [2]

In the adult form clinical manifestations generally appears after 2 years of age. The classical triad of abdominal pain, palpable abdominal mass and jaundice may be seen in a few patients . Older patients may present with cirrhosis and manifestation of portal hypertension.[3] Differential diagnoses are included congenital hepatic fibrosis, primary sclerosing cholangitis, congenital cirrhosis and congenital stricture of common hepatic or common bile duct and biliary atresia. [4] Ultrasonography is a good screening test followed by hepatobiliary iminodiacetic acid (HIDA) scan.Diagnosis can also be made in second and third trimester

of pregnancy on routine antenatal ultrasonography. [5,6]Computed Tomography (CT) scan is reserved for a patient with intrahepatic billiary cyst. Peroperative cholangiography in children provides the most accurate anatomical information but is not routinely performed being limited for selective cases. The standard treatment is surgical excision of the cyst and Roux-en-Y hepatico Jejunostomy.[7, 8]

Biliary complications may develop after surgery and are usually seen as anastomotic stricture or primary ductal stricture. Liver histological findings in choledochal cysts vary with age. In the new born, liver histology is normal or mild ductal proliferation and fibrosis may be noted. [9] Early diagnosis and surgical treatment is necessary as it prevents development of liver changes. [10]

Patients and Methods

After approval from ethical committee, this prospective , multi-institutional trial was conducted t

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King Edward Medical University and Children Hospital & Institute of Child Health, Lahore. The duration of study was 11 years, from January, 2004 to December, 2015. All the patients presenting with diagnosis of Choledochal cyst were included in the study. Presenting symptoms, diagnostic strategy and treatment provided were recorded. In all of these patients, along with surgical treatment of CC, liver biopsy was taken per-operatively. Histopathology reports were reviewed by two senior histopathologists who were not informed about age of the patients (single blind study).Results were analyzed by using SPSS 21. Software and spearman's correlation tests were used to find out any significant relationship between cirrhosis on histology and age of the patients at presentation.

Results

A total of 53 patients were included in the study. The patients included mainly belonged to age group 2 -5 years (47.16%) followed by 5-12 years (33.96) and lastly less than 2 years (18.86%). The main sign and symptoms with which the patients presented were jaundice (n=42), abdominal pain (n=33) and fever (n=29). Other complaints were hepatomegaly (n=17), palpable mass (n=36) and vomiting (n=16). Less common symptoms were splenomegaly (n=10), itching (n=03), nausea and bleeding per rectum (n=01). Abnormally long extra hepatic left duct and abnormal arterial pattern were the commonest associated anomalies (Table 1). Blood Counts and liver function tests were performed in all patients and level of conjugated bilirubin were found raised with mean 3.4+2.72 mg/dl. Ultrasound was the initial screening examination of choice in patients with choledochal cyst. Ultrasound was diagnostic in most of the cases (n=48) with intrahepatic dilation in three. In these three patients finding were confirmed by per operative cholangiography. Doubtful findings were noted in two patients in whom CT Scan was done and in one patient HIDA scan was done who showed distal common bile duct obstruction. Also in 5 patients diagnosis of CC was made on CT scan.

Complete excision and primary Roux en Y hepatico-jejunostomy was done in 53 patients. Peroperatively all cysts (n=53) were found to be of Type –I with Sacular (n=48) and tubular (n=5) subtypes. Macroscopic cirrhotic changes were noted in 5 patients but liver biopsy was taken in all patients .In histopathology cirrhotic changes were noted(Figure 1). Correlation of histologic findings with patient's age were evaluated using Spearman's correlation test. Significant relation was found between all variables except for billiary cinhosis which showed p=0.015 R=0.897 in patients above 2 years of age. A significant association of age of the patient with presence of billiary cirrhosis(Table 2&3). Associated histopathological features were also studied (Table 4). By using spearman's correlation test, their association with age of the patient was assessed. There was association of cirrhosis with increasing age of the patient and statistical significance (p< 0.015) was found

Table-1: Choledochal cyst --Anomalies noted

Anomalies	No(%)
Abnormally long extra hepatic left duct	02 (05.55%)
Abnormal arterial pattern	02 (05.55%)
Congenital hepatic fibrosis	01 (02.77%)
Accessory hepatic duct	01(02.77%)
Absent Rt. Kidney	01 (02.77%)

Table 2: Stratification of cirrhotic changes according to age of patients (Upto 2 years)

Age in years	No. of Cases having Biliary Cirrhosis	No(%)	Percentage
< 1 year	03	06	50%
1-2 year	02	04	50%
Total	05	10	50%

Table 3: Stratification of cirrhotic changes according to age of patients (More than 2 to 5 years)

Age in years	No. of Cases having Biliary Cirrhosis	No (%)
>2-3	3	7(42.85)
3-4	5	9(55.55)
4-5	6	9(66.66)
5-7	4	7(57.14)
7-9	4	5(80)
9-12	5	6(83.33)
Total	27	43(63.0)

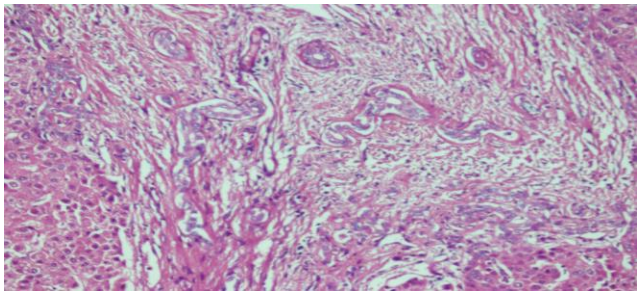

Figure 1: Expanded portal area with increased bile duct proliferation and early cirrhotic changes.

Table 4: Choledochal cyst- Histological findings in association with cirrhosis

Associated finding	Percentage
Giant cell transformation	22
Parenchymal cholestasis	56
Parenchymal inflammation	42
Extramedullary haemopoiesis	5.5
Portal inflammation	47.2
Portal fibrosis	66.6
Proliferation of bile ductules	64

Discussion

Relationship between various histopathological features in the specimen of the liver biopsy of the patients with choledochal cysts to their age was determined. In our study, 58 patients were diagnosed to have choledochal cyst and 53 underwent hepatico Jejunostomy. These 53 patients were subjected to liver biopsy. We found that delay in diagnosis was mainly due to lack of awareness and non availability of expert ultrasonologist at the primary health care level, which is necessary for early referral and prompt treatment.In the present study, children less than 2 years presented mainly with history of jaundice (n=10) and fever (n=10). On clinical examination, hepatomegaly (n=6) and palpable abdominal mass was found (n=10). Splenomegaly was found in 50% of the cases under 2 years of age (n=5). Similar findings were found in a study conducted in Thailand in which jaundice was the most common symptom in infant among 74 paediatric patients of similar disease. [11]

Children more than two years of age mainly presented with abdominal pain (76.66%). There was also history of jaundice, which was episodic (53.33%). Vomiting of non bilious nature was found in half of the patients in this group. Other clinical findings were palpable abdominal mass, hepatomegaly and history of clay colored stool in 30% of cases in this group. Similar results were found in a study conducted by Devries et al in Netherland. They studied 42 patients and 76% patients older than 2 years presented with abdominal pain in their study. [12]

In our study, female predominance was noted with female to male ratio being 3.5:1 and anemia was found in 78% of cases. Conjugated bilirubin level was raised in 64% of cases with highest level being 9.8gm/dl. Alkaline phosphatase was also raised in 61% of patients with range being 205 IU /L to 1950 IU/L. Similarly AST, prothrombin time was raised in 56% and 20% of cases respectively. Similar results were found in another study conducted in Japan by Suita and Shono k et al. [13]

Abdominal ultrasound was done in all the cases and was found diagnostic in most of the cases. Similar results were found in another study on 34 patients conducted in India and in a study on 24 Chinese infants and children in whom ultrasound was found to be rapid and accurate diagnostic method for initial evaluation. [14, 15] Biliary cirrhosis was found in 50% of cases (5 out of 10) in patients of less than 2 years of age. Biliary cirrhosis was found to be increasing with increasing age above 2 years age. Similar histopathological findings were noted in a study conducted by Nambirajan and Taneja et al on 22 Paediatric patients. [16]

Ishimaru and Kitano et el have studied liver histology not only at the time of operation but post operatively at 04 months and 01 year of age by fine needle technique and had noted improvement. Even normal looking liver showed evidence of significant changes. Presence of cirrhosis, more common in infants, correlated with jaundice and deranged liver function tests. [17]

Changes in pre existing liver cirrhosis after biliary decompression are also studied by Jackson and Wv et el on 47 patients as comparative study and Gong ZH and Xia et al have done immune histochemical assessment of liver fibrosis to get and indicator for post operative prognosis. [18, 19] Similar study was conducted by Fumino and Higvchi et al on 15 patients of choledochal cyst and liver biopsy was analyzed for fibrosis & cirrhosis. They also focused on the type of choledochal cyst in relation to advanced liver fibrosis on H & E stain and noted grade 3 & 4 fibrosis in type IV a. [20]

Conclusion

1.There is a significant relationship between increasing age of the patient with choledochal cyst and cirrhotic changes in their liver. Above 2 years of age, biliary cirrhosis was found in 63% of the patients of choledochal cyst.

2.Prompt diagnosis and early treatment of choledochocal cyst is necessary to avoid development of these irreversible changes in liver.

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