

CHILDHOOD CIRRHOSIS OF THE LIVER(*)

A Histopathological and Histochemical Study of 39 Cases

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SUMMARY: *Childhood cirrhosis of the liver:* Retrospective analysis of the biopsy and necropsy files in the Department of Pathology of Istanbul (Çapa) Medical Faculty during the years 1934-1980 revealed 39 cases of childhood cirrhosis. All cases were histopathologically and histochemically reassessed. Distribution of the cases according to aetiology showed the following results: Biliary 11 cases (28 %), Posthepatic 6 cases (15 %), Nutritional (portal) 6 (15 %), Genetic-Metabolic 4 (10 %), Cardiac 4 (10 %) and Unspecified 8 (20.5 %). The main cause of biliary cirrhosis was due to extrahepatic conditions. In the group of genetic-metabolic aetiology, there were 3 cases of Wilson's disease and one case of glycogenosis Type IV (Andersen's disease).

INTRODUCTION

Cirrhosis of the liver is uncommon in children. All the hepatic conditions occurring in childhood can progress to cirrhosis. While biliary, genetic-metabolic, nutritional (portal), posthepatic and vascular factors are considered responsible in the aetiology, sometimes, no cause is apparent as in "cryptogenic" cirrhosis (2,4,5). In this study, 39 cases of childhood cirrhosis were presented, and their aetiological, histopathological and histochemical features were discussed.

MATERIALS AND METHODS

Retrospective analysis of the biopsy and necropsy files in the Department of Pathology of Istanbul (Çapa) Medical Faculty during the years 1934-1980 inclusive revealed 39 cases of childhood cirrhosis. 23 of these were biopsy and 16 were necropsy cases. One of these cases, which was a case of glycogenosis Type IV (Andersen's disease), had been previously reported (1).

Frosh sections were prepared from the old paraffin blocks of specimens and stained with hematoxylin and eosin; silver impregnation for reticulin, PAS for glycogen, mucin; PAS with diastase specific for non-glycogen mucopolysaccharides and Orcein for copper and hepatitis B virus (HBV) antigen. All were examined by standard light microscopy.

RESULTS

1139 cases of cirrhosis (biopsy and necropsy) had been established in the Department of Pathology of Istanbul Medical Faculty during the years 1934-1980. Of these, only 39 cases (3.4 %) belonged to the age group of 0-12 years which was included into our study.

10 cases were between 0-11 months and 29 were between 1 and 12 years old. 25 cases were males and 14 were females. TABLE 1 shows the distribution of our cases by aetiology, age and sex.

Most of the cases were biliary cirrhosis (11 cases, 28 %). According to data available in the reports, underlying causes were established in 10 of the 11 cases (TABLE 2). In two cases, neonatal hepatitis was also found to have associated with biliary cirrhosis.

Of the 4 cases with genetic-metabolic origin, 3 were Wilson's cirrhosis and one was glycogenosis Type IV (Andersen's glycogen storage disease). In all of the 3 cases of Wilson's cirrhosis, protein-bound copper was detected at the levels of (++) and (+++) with orcein staining (FIGURE 1 and 2).

In 6 cases of cirrhosis with posthepatic origin, 5 cases were due to chronic hepatitis. In one case, the cause was not specified. On the otherhand, orcein stain did not reveal any histochemical findings in relation with HBV.

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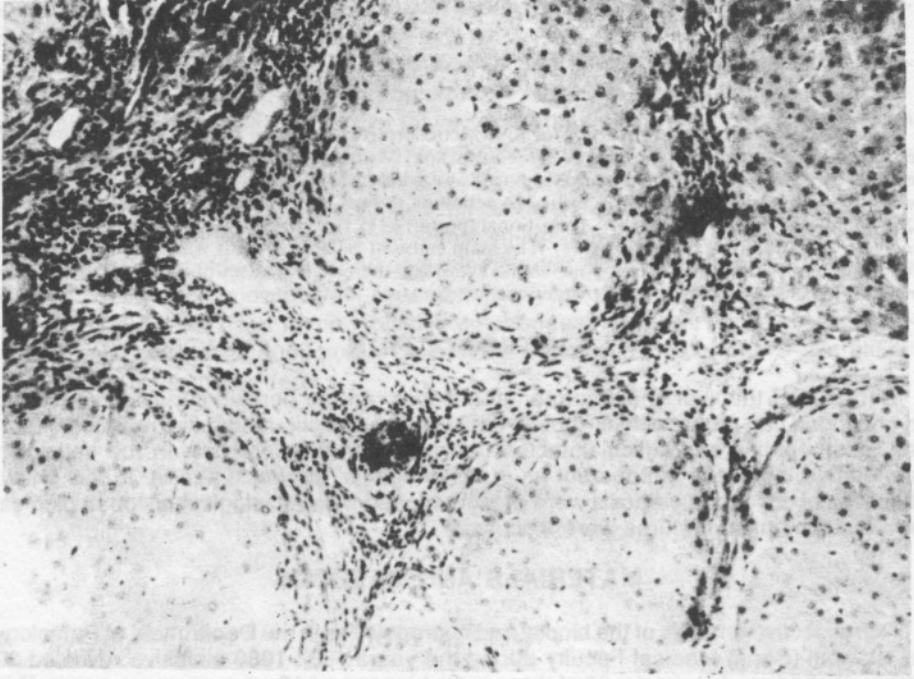


FIGURE 1. Cirrhosis in Wilson's disease is usually the macronodular type showing variable large nodules limited by thin fibrous bands and chronic inflammatory reaction in periportal areas. (Case no: 324/61, H. and E stain, 125 x).

In 4 cases with cardiac origin, one case was due to constructive pericarditis. Although heart failure was responsible, no definitive cardiac-vascular aetiology was noted in other 3 cases.

DISCUSSION

In our study, it was found that most of the cases were biliary cirrhosis (11 cases, 28 %). The commonest cause of biliary cirrhosis in childhood is attributed to atresia of the extrabiliary bile ducts (5). In this study, atresia of the extrabiliary bile ducts was found in 4 of the 10 cases (40 %) of biliary cirrhosis, but in general, 7 out of the 10 cases (70 %) were due to extrahepatic causes. In 2 cases, the cause was noted as atresia of the bile duct without any indication of 'intra' or 'extra'. All of our cases, which were caused by an obstruction in some part of the bile duct system, were secondary biliary cirrhosis. Primary biliary cirrhosis rarely occurs in individuals under 30 years of age, and it mostly occurs in middle-aged females (4,5). Except two cases (one was due to involvement of the common bile duct by lymphoma and the other one was a case liver tumour), all the biliary tract conditions were congenital in our cases. The other causes of biliary cirrhosis such as mucoviscidosis and deficiency of α -1 antitrypsin were not encountered in the study. PAS with diastase stain did not reveal any PAS (+) diastase resistant granules characteristic for α -1, antitrypsin locked in liver cells.



FIGURE 2. Protein bound copper is demonstrated as dark intrahepatoeytic granules with Orcein stain in Wilson's disease. (Case no: 324/61, Orcein stain, 500 x).

The most common histopathological findings in the cases of biliary cirrhosis were portal fibrosis and micronodules (nodules of almost equal size not exceeding 3 mm in diameter), proliferation of bile ducts and bile retention in the lobules.

We had 3 cases of Wilson's disease and one case of a special type of a glycogen storage disease (Andersen's disease). Wilson's disease is suggested by neurological signs (tremor, dysarthria, deteriorating performance at school, Kayser-Fleisher rings) in a child over the age of 6 years with marked hepatocellular insufficiency. It appears to be an inherited disturbance of copper metabolism. Increased accumulation of copper is found in the liver, brain, kidney and cornea. We detected protein-bound copper with the levels of (**) and (***) in the liver with orcein staining. Histopathology showed macronodular type of cirrhosis. All of our 3 cases were above 6 years.

Of the 6 cases of posthepatic cirrhosis, 5 were due to chronic hepatitis. Cirrhosis following acute hepatitis A or B or the other infectious causes of hepatitis, such as rubella and cytomegalovirus, usually cannot be distinguished from each other histologically (5). We were not able to demonstrate HBV antigen in the liver by means of orcein staining in our cases.

Nutritional cirrhosis (Laennec's cirrhosis, portal cirrhosis) occurs most commonly in middle life but it is also seen in children. The aetiology is still debated. Certain poisons such as carbon tetrachloride, tars, phosphorus, chloroform and dietary deficiency i.e. aminoacid have been found as causative or contributing factors (5). Portal cirrhosis due to alcoholism is unusual in children (2).

Table 1. Distribution of our cases of childhood cirrhosis by aetiology, sex and age.

Aetiology	Age		Sex		Necropsy	Biopsy	Total
	0-11 months	1-12 years	M	F			
Biliary	9	2	3	8	4	7	11 (28.2 %)
Nutritional (portal)	1	5	6	—	2	4	6 (15.3 %)
Posthepatic	—	6	6	—	1	5	6 (15.3 %)
Genetic-Metabolic	—	4	2	2	4	—	4 (10.2 %)
Cardiac	—	4	3	1	4	—	4 (10.2 %)
Unspecified	—	8	6	2	1	7	8 (20.5 %)
Total	10	29	25	14	16	23	39

Table 2: Distribution of underlying causes in 10 cases of biliary cirrhosis.

Cause	No. of cases
Atresia of the extrahepatic bile ducts	4 (x)
Atrophy of the extrahepatic bile ducts	2
Aplasia of the extrahepatic bile ducts	1
Atresia of the bile ducts	2 (xx)
Intrahepatic bile duct obstruction due to liver tumour	1
Total	10

(x) In one case, atresia was due to involvement of the common bile duct with lymphoma.

(xx) neonatal hepatitis was found to have associated in both cases.

Centrizonal hepatic cell necrosis occurs in all forms of heart failure with prolonged passive congestion and anoxia. Then central fibrosis results. It is most commonly associated with constructive pericarditis and rheumatic heart disease. In our 4 cases of cardiac cirrhosis, we were able to find the underlying cause only in one case. It was a case of constructive pericarditis. The causes in other 3 cases of heart failure were not noted.

In a study of 72 cases, Özsoylu et al. (3) found the following results in relation with childhood cirrhosis: 17 cases of postnecrotic cirrhosis (23.6 %), 8 biliary cirrhosis (11 %), 6 portal (8.3%) and 7 Wilson's disease (9.7%). In 34 cases (47%), type was not specified. The number of unspecified cases were 8 (20.5 %) in our cases.

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