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CONGENITAL HEPATIC FIBROSIS IN TURKISH CHILDREN*

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Cirrhosis is the most frequent cause of portal hypertension in childhood in Turkey[1], and idiopathic portal hypertension (IPH: portal hypertension with normal liver morphology, function and spleneportogram) is the second most frequent entity[2]. Extrahepatic obstruction such as thrombosis in the portal system is the third factor to be considered in cases of portal hypertension in Turkey[2].

There are other relatively rarer causes of portal hypertension. Congenital hepatic fibrosis (CHF) is one of them but in Turkey this is actually not so very infrequent and this is probably a result of the frequency of intermarriage.

Material and Methods

Twenty-four patients with CHF were examined. The ages of the patients ranged from four months to 15 years at the time of diagnosis, with a mean of 5.4 (and median 5.5) years. Six of them were girls and 18 were boys. Diagnosis was made by liver biopsy by using Vim Silverman needle[3] in 21 and surgery in five cases; in two by both methods. In addition, splenoportography, esophagrography and intravenous pyelography were performed in patients 11, 12 and 18 respectively. In all of the patients, family histories were reviewed and liver function tests were taken; SGOT, SGPT, alkaline phosphatase, total protein with albumin, bilirubin, prothrombin time (PT), partial thromboplastin time (PTT), complete blood counts and urinalysis were carried out by routine laboratory methods. Serum HBsAg was determined by using counter immunoelectrophoresis[4].

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Results

The main complaint of the patients was abdominal enlargement which was noticed between the newborn period and 12 years of age with the mean age of three years (median two years). Abdominal enlargement was observed in the newborn period in five patients. At the time of examination hepatomegaly, according to the criteria of Deligeorgis et al[5], was present in all patients; the liver being 2-12 cm below the right costal margin. The enlargement of the left lobe (with a harder consistency) by 3-10 cm was found in 17 cases. Splenomegaly, extending 2-18 cm below the left costal margin was present in 18 of the cases. One patient also had kala-azar at the time of diagnosis. Ascitis was detected clinically in one patient only, and there was mild arterial hypertension in two patients; 130/70 Hg in a five-year-old boy and 140/80 Hg in a three-year-old girl.

There was a history of melena in eight and of hematemesis in seven patients. There was consanguinity of the parents in 11 cases; two of the cases were siblings.

Eleven of the patients were underweight; four were below the 25th percentile, three below the 10th and four below the 3rd with respect to their ages. Stunted growth was also present in 20 patients; two were below the 25th percentile, five below the 10th and thirteen below the 3rd.

Hemoglobin values ranged from between 4.6 and 13.4 g/dl and in 12 it was less than 10 g/dl. White blood cell counts were between 1300 and 5200/μl and leukopenia (<5000/μl) was detected in five. SGOT and SGPT values were found mildly elevated (100 and 150 μ) in only two patients.

Prolonged prothrombin times (>12 secs) and thromboplastin times (>120") were found in five patients; two patients had hypoproteinemia (>5 g/dl) and three hypoalbunemia (>3.5 g/dl).

In five patients proteinuria was shown and HBsAg was present in one. For seven patients the BUN and creatinine levels were determined; only in one case, that of the patient being treated for kala-azar, were the levels elevated (BUN 25 mg/dl; creatinine 1 mg/dl).

Esophagograms were taken of 12 patients and in 5 varices were revealed; the youngest was 3.5 years of age. Elevated splenic pulp pressure (>200 mm/Hg) and venous collaterals were found in all 11 patients on whom a splenoportography was carried out; the youngest one was four months of age. In five patients only, intravenous pyelography revealed no pathological sign; in the rest enlarged kidneys with tubular ectasia were seen.

In liver biopsies, hepatic lobular architecture was found to be well preserved and diffuse or focal nodular proliferation was not seen. Bizarre intrahepatic proliferations of lobular bile ducts, occasionally forming microcystic dilatations and

surrounded by cellular mesenchymal fibrous tissues, were diagnostic. There was no inflammatory infiltration in portal areas (Figure 1). There was well-deliniated dense fibrosis and within the fibrosis multiple and irregular cavities lined with biliary epithelium were observed. Fibrosis was more prominent in 13 of our patients and cystic lesions in 11 of them[5]. A close follow-up was not possible with most of our patients but as far as we know only two have died, both of gastrointestinal bleeding. Two of the patients in the longest follow-up group, aged seven and eight years, had more cystic lesions. Another ten patients to be fairly closely followed up had no major complications; these were equally divided between the cystic and fibrotic groups. So among our patients prognosis did not seem to relate much to the type of liver morphology. Despite gastrointestinal bleeding, only two of the patients had a splenorenal shunt operation. In seven patients this could not be performed because of the size of the vessels. In one patient cholongitis was observed and the surgical treatment for that patient was successful and has been described in detail elsewhere. As to the associated findings in these patients, there was one case of kala-azar and one with HBsAg positivity.

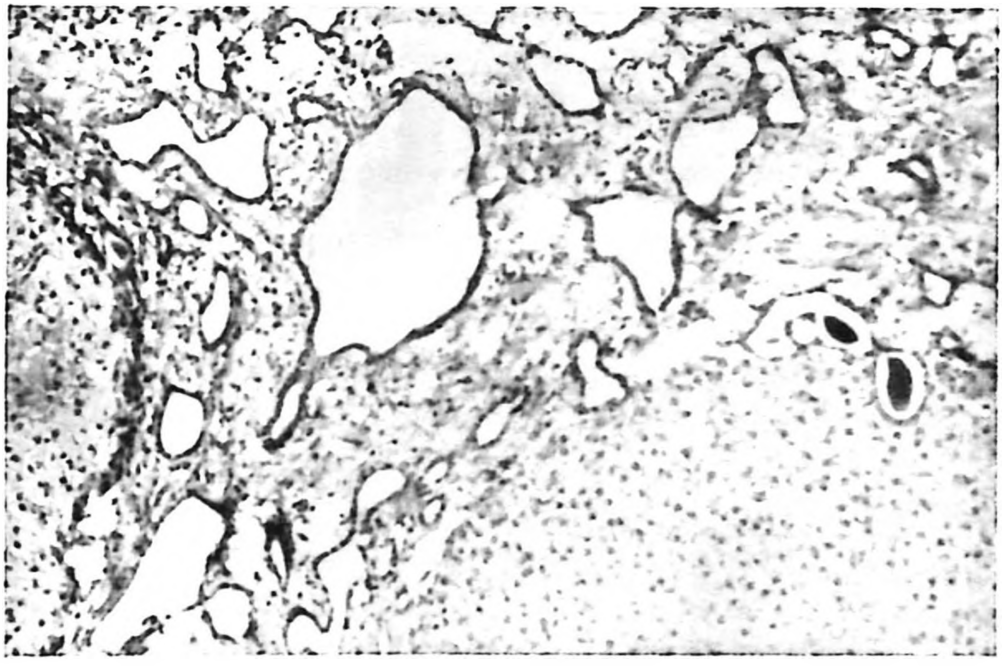

Figure 1

Hyperplastic portal biliary ducts embedded in expanded portal spaces, with no histologic evidence of proliferation of hepatic cells.

Discussion

Hepatomegaly, especially prominent in the left lobe, splenomegaly, consanguinity of the parents or the presence of similar cases in siblings are all useful factors in the diagnosis of CHF[6]. In this entity, characteristics include hepatomegaly caused

by fibrosis, normal liver function tests, and portal hypertension with gastrointestinal bleeding[7,8]. Fibrosis is the major abnormality but cysts which are a segmental dilatation of the bile ductus or proliferation of bile ducts are also usually present. Thus the typical histopathology is quite distinct from that of cirrhosis. Although fibrosis is the major pathology, in some cases cysts may also be prominent. In this cystic form other organs such as spleen, pancreas, ovary and lungs should also be checked for polycystic lesions. Fibrosis of the intrahepatic branches of the portal vein cause portal hypertension. CHF is usually associated with kidney involvement, characterized histologically by tubular dilatation in the medulla and cortex which can give a radiological image of tubular ectasia. In some patients renal involvement is compatible with polycystic kidneys and may increase the risk of renal failure[9-12].

The major clinical problems related to this entity are portal hypertension, hypersplenism and renal failure. Hematemesis and melena are the most common complications of hypertension and these usually determine the prognosis. Bleeding and hypersplenism were present in at least half of our patients and as a result anemia was not uncommon. Patients usually require blood transfusions following bleeding episodes but a preferable approach should be portocaval anastomosis. Death can also occur as a result of anuria and renal failure. Such relatively frequent complications were not in fact observed among our patients, but it seems that patients with polycystic kidneys were referred to the nephrology section. If the livers of these patients were morphologically examined more patients with CHF would be found.

The high frequency of consanguinity (about 46%) between the parents of these patients suggests that there is recessive inheritance with this disorder. Certain differences in liver pathology in two siblings, one being more cystic and the other more fibrotic were found in this series; similar cases had been observed previously[5]. Portal hypertension was documented in one of our patients who was four and half a months of age. This condition had been previously reported in the neonatal period[13].

Although duplication of intrahepatic branches of the portal vein has been shown on splenoportogram by Alvarez et al[14], in most of their CHF patients this was not the case with our patients. Stunted growth was observed in 83% of our patients and poor weight gain in 46%. Carolis syndrome with intrahepatic biliary dilatation without portal fibrosis should be differentiated from congenital hepatic fibrosis which is not familial and in which the kidneys are not involved[15].

Acute and latent chronic cholangitis with fever, abdominal pain and jaundice is a rare but important complication of this entity[14,16] and was documented in one of our patients.

Summary

Twenty-four cases of congenital hepatic fibrosis are presented. There was hepatomegaly, the enlargement of the left lobe in 17 cases, splenomegaly in 18 cases, hematemesis in 7 cases, and melena in 8 cases; further there was consanguinity of the parents of 11 patients. In the liver biopsies fibrosis was more prominent in 13 patients and cystic lesions in 11 of them. It should be stressed that congenital hepatic fibrosis should be considered among the causes of portal hypertension in childhood and should be distinguished from cirrhosis.

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