CONGENITAL HEPATIC FIBROSIS: A CASE REPORT AND FAMILY STUDY*

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Congenital hepatic fibrosis was first described by MacMahon in 1929[1] and since that time about 100 cases have been reported. Kerr *et al.*[2] published an excellent review in 1961. This disease is characterized by an extremely firm enlarged liver resulting from diffuse periportal fibrosis, which distorts but does not basically alter the lobular architecture. There is associated bile duct proliferation with cyst formation and a paucity of portal vein radicles. A significant number of cases have associated congenital renal cysts. We wish to report a case which presented all the characteristic features. A study of the patient's family was also undertaken, because of the reported familial incidence in this disorder. Definite hepatic or renal abnormalities were found in 3 other members of the family.

CASE REPORT

A Coloured male was first admitted to this hospital in May 1957 at the age of 30 years. He was found by his general practitioner to have an asymptomatic large liver and spleen. On examination, the only abnormality found was a 3-finger, very hard, non-tender hepatomegaly and a 5-finger, non-tender splenomegaly. The following were the results of blood tests at that time: haemoglobin 11·0 G/100 ml.; ESR 10 mm. in the first hour; serum albumin 4·4 G/100 ml.; serum globulin 2·8 G/100 ml.; bilirubin 0·5 G/100 ml.; thymol turbidity 5 units; zinc turbidity 16 units; and prothrombin index 96%. The patient refused a liver biopsy and was discharged. A clinical diagnosis of Banti's syndrome was made.

His second admission was in January 1966. On the day before admission and on the day of admission he developed epigastric pain and haematemesis. He had never been a heavy drinker. On examination he was found to be drowsy. The blood pressure was 130/70 mm.Hg and the pulse rate 110 per minute. Special investigations on this occasion showed the following: blood urea 150 mg./100 ml.; bilirubin 1·2 mg./100 ml.; alkaline phosphatase 8·0 units; thymol turbidity 0; zinc turbidity 2; and serum glutamic oxaloacetic transaminase 28.

On the day after admission, the patient lapsed into a moderately deep coma and was given an exchange transfusion of 10 pints of blood. However, his condition deteriorated rapidly. He had a grand mal seizure, his temperature rose to 103°F and his blood pressure fell to 70/45 mm.Hg. His death was considered to have resulted from another episode of gastro-intestinal haemorrhage.

Postmortem Findings

The liver (1,972 G) was extremely hard and moderately enlarged. The initial impression was that of a fine portal cirrhosis, but on close inspection this was seen to be erroneous. The capsular surface showed a uniform fine nodularity and the cut surface a complex pattern of anastomosing bands of liver cells measuring 2 - 4 mm. in thickness. These bands were surrounded by dense fibrous septa measuring up to 1·0 mm. in thickness (Figs. 1 and 2). Histologically, the liver cell bands were composed of hypertrophied lobules but not of regenerative nodules as shown by the preservation of normal central veins and portal tracts. This was particularly well seen with reticulin

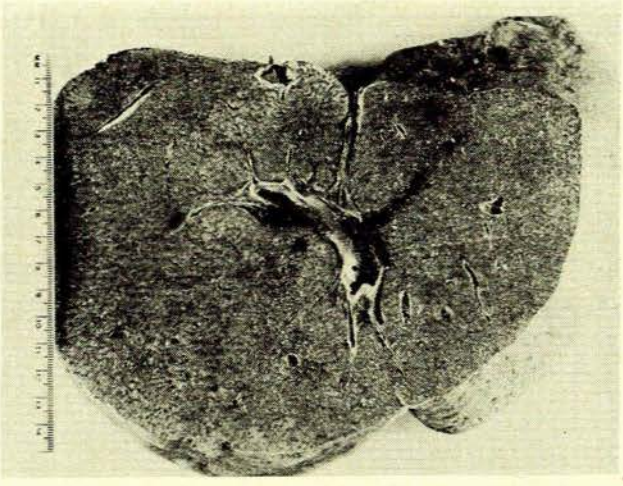

Fig. 1. Liver showing complex pattern of anastomosing bands of liver cells separated by fibrous septa. The appearances superficially resemble that of a uniform portal-type cirrhosis.

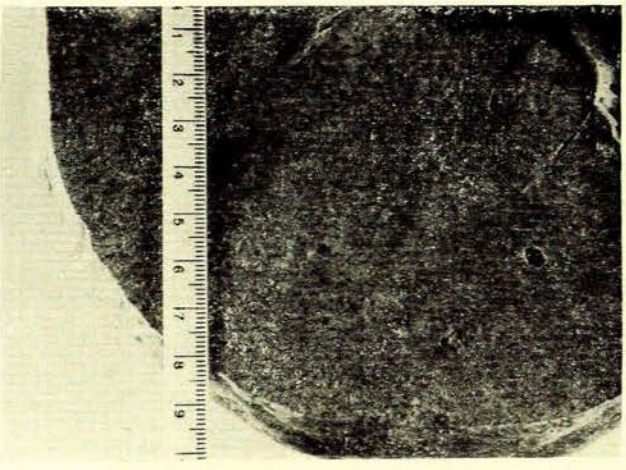

Fig. 2. Greater detail of the cut surface of the liver. The uniform width of the liver cell bands and of the fibrous septa is shown.

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stains (Fig. 3). The gross architectural distortion was the result of the presence of dense fibrous septa separating the bands of liver cells. A very sharp transition line was

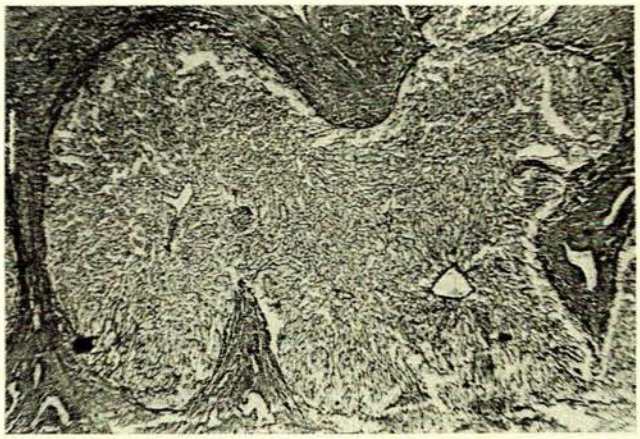

Fig. 3. Reticulin stain showing preservation of central veins within the liver cell bands. The sharp transition between liver cells and fibrous tissue is also shown (reticulin stain × 50).

present between the liver cells and fibrous tissue (Fig. 4). Within this dense fibrous tissue there were numerous bile ducts which varied considerably in size. Some resembled large interlobular ducts and others small intralobular ducts of Hering. The outlines of many of the larger ducts were irregular and about one-quarter contained laminated bile plugs (Fig. 5). The bile plugs had caused pressure atrophy and even disappearance of the lining epithelium of some of the ducts. The hepatic arteries were normal in size and frequency, but the portal vein radicles were sparse and irregular in shape.

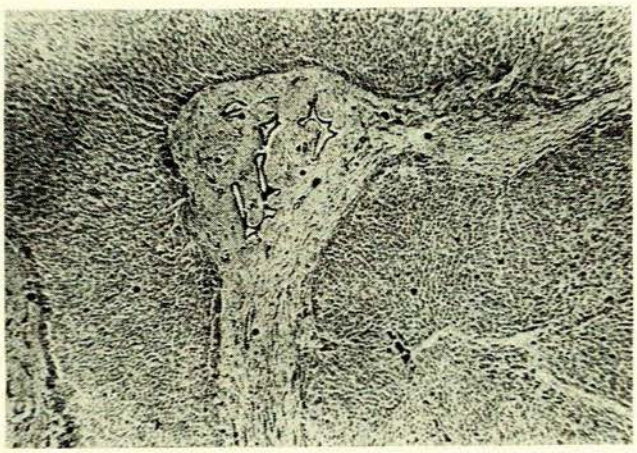

Fig. 4. Bands of liver cells and fibrous septa very clearly demarcated from one another. Numerous irregular bile ducts are seen within the fibrous septa (H & E × 50).

The kidneys (387 G) contained scanty cystic areas in both the cortices and medullae (Fig. 6). These cysts were variable in size, measuring up to 0·5 cm. in diameter, and they had smooth, round outlines. They were seen histologically to be much dilated and tortuous tubules lined by a single layer of cuboidal epithelium (Fig. 7).

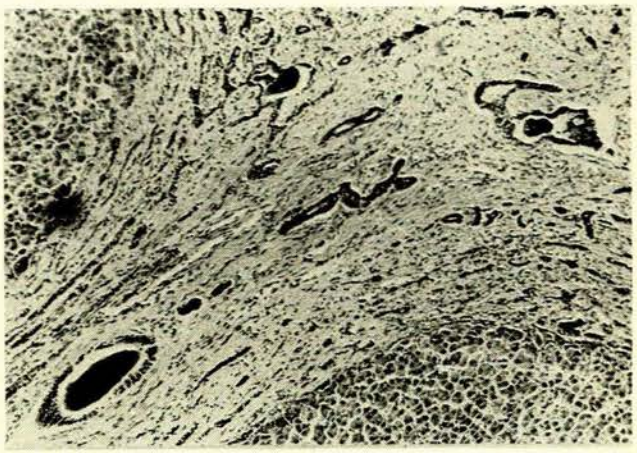

Fig. 5. Greater detail of the numerous bile ducts, some containing inspissated bile plugs (H & E × 100).

Fig. 6. Kidney showing cystic spaces in both the cortex and medulla.

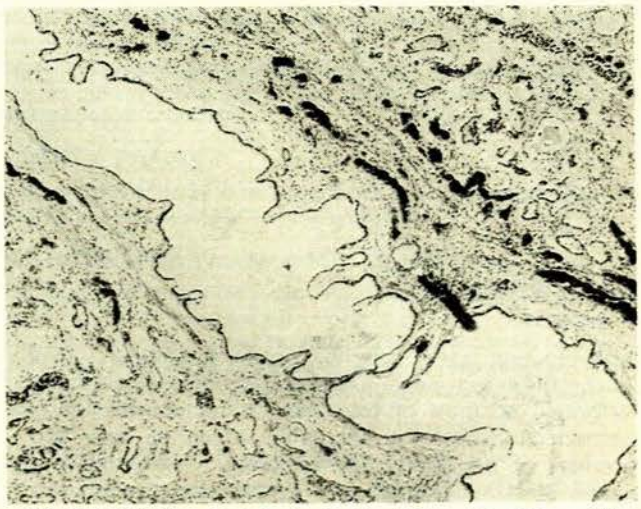

Fig. 7. Dilated cystic tubules in the kidney (H & E × 90).

The spleen (1,443 G) was very large and firm with capsular thickening.

Large, distended and tortuous varices were present at the lower end of the oesophagus. The stomach and small bowel contained a large amount of altered blood.

There were no other significant abnormalities. The final anatomical diagnoses in this case were: congenital hepatic fibrosis, oesophageal varices, congestive splenomegaly (clinically portal hypertension) and congenital renal cysts.

Family Investigation

In view of the well-documented occurrence of familial incidence in congenital hepatic fibrosis, we studied 17 members of the proband's family (Table I and Fig. 8).

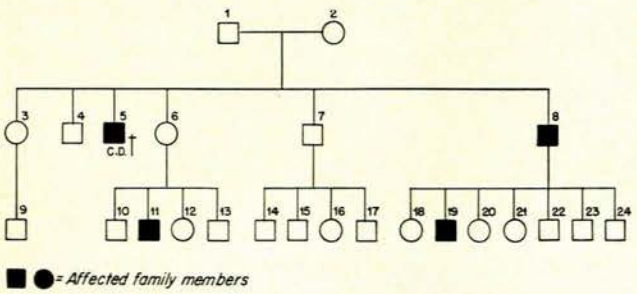

Fig. 8. Family tree of patient.

TABLE I. RESULTS OF STUDY OF PATIENT'S FAMILY

Family members	*Barium swallow*	*Intravenous pyelogram*	*Liver-function tests*
1	+	+	+
2	—	+	+
3	—	+	+
4	—	—	+
5 (patient)	—	—	+
6	—	+	+
7	—	—	—
8	—	*	—
9	—	+	+
10	—	+	+
11	+	+	*
12	—	+	+
13	—	—	—
14	—	+	—
15	—	+	—
16	—	+	—
17	—	—	—
18	—	+	+
19	—	*	—
20	—	—	—
21	—	—	—
22	—	—	—
23	—	+	—
24	—	—	—

— = test not performed.
+ = test performed but normal.
* = test performed and abnormal.

Liver-function tests, including bromsulphthalein retention and prothrombin index, and intravenous pyelograms were performed on most of the cases. A barium swallow was performed on 2. From the table it can be seen that 2 members of the family had abnormal intravenous pyelograms. Both had radiological deformities consistent with congenital cystic kidneys. A third member of the family had a raised alkaline phosphatase level of 17 units and a prothrombin index of 89%.

DISCUSSION

Congenital hepatic fibrosis is an uncommon disorder in which a familial incidence has been recorded on several occasions. Kerr *et al.*[2] reported 13 cases of this disease, including 3 siblings in one family. Campbell *et al.*,[3] Van der Schoot[4] and Ivemark *et al.*[5] have also reported cases affecting 2 or more siblings. Kerr *et al.*[6] surmised that the mode of inheritance was probably recessive, but sufficient data are as yet not available. Of 17 members of the family studied above, two had pyelographic findings suggestive of congenital renal cysts, and one other member of the family had a raised alkaline phosphatase level. The liver-function tests in this disorder are invariably within normal limits, except for the alkaline phosphatase which is occasionally elevated. Portal hypertension with development of oesophageal varices is the single most important complication, and is the usual cause of death. These individuals are very suitable candidates for portacaval shunt operations because of their excellent liver function. Eight of 13 cases reported by Kerr had successful shunt operations and they remained alive and well 3 years or more after the procedure. We were able to perform a barium swallow in only 2 members of the family, in both of whom this was within normal limits.

The liver in congenital hepatic fibrosis is extremely firm and moderately enlarged. Its firmness is often the cause of unsuccessful attempts at obtaining specimens for biopsy. Although it grossly resembles a fine portal cirrhosis, the fibrous septa impinge upon hepatic parenchyma in which a normal spatial relationship of central veins and portal tracts is maintained. This is best demonstrated with silver stains. The fibrous bands obviously distort the normal architecture, but regenerative nodules are not formed. Within the fibrous bands an adequate number of hepatic arteries are present but portal vein radicles are sparse. It is not known whether the paucity of portal vein radicles is the result of compression of the vessels by fibrous tissue or a primary hypoplasia. In any event, portal circulation is compromised and portal hypertension results. The fibrous bands contain numerous small and large bile ducts, many of which are distorted and some of which contain inspissated bile plugs. Despite this distortion of the biliary tree, very adequate biliary drainage must still be present as jaundice occurs very infrequently.

The hepatic fibrosis and bile duct hyperplasia are considered to be a developmental disturbance. Formation of intrahepatic bile ducts is dependent on an ingrowth of connective tissue from the porta hepatis, so that associated disturbances of bile duct proliferation and fibrous tissue overgrowth are not surprising. The association with congenital renal cysts is further evidence of the developmental nature of the disorder. Three of the 13 cases reported by Kerr *et al.*[2] had congenital renal cysts. Some authors believe congenital hepatic fibrosis to be a variant of congenital cystic liver, as both are associated with hyperplasia and cystic dilatation of bile ducts and with congenital renal cysts. However, excessive fibrosis and the development of portal hypertension are not features of congenital cystic liver.

SUMMARY

Congenital hepatic fibrosis is a rare cause of otherwise unexplained hepatomegaly and portal hypertension in children and young adults. The recognition of the disorder is of importance in that these patients would be suitable candidates for portacaval shunts since liver function is usually very adequate. The familial occurrence noted in several instances indicates the need for investigation of the family of the affected proband. The case reported here was diagnosed only at autopsy, but subsequent investigations of the family have shown 2 members with pyelographic findings suggestive of congenital cystic kidneys and one with a raised alkaline phosphatase level which may indicate underlying liver disease.

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REFERENCES

1. MacMahon, H. E. (1929): Amer. J. Path., **5**, 499.
2. Kerr, D. N. S., Harrison, C. V., Sherlock, S. and Walker, R. M. (1961): Quart. J. Med., **30**, 91.
3. Campbell, G. S., Bick, H. D., Paulsen, E., Sober, P. H., Watson, C. J. and Varco, R. L. (1958): New Engl. J. Med., **259**, 904.
4. Van der Schoot, J. B. (1955): Ned. T. Geneesk., **99**, 2579.
5. Ivemark, B. T., Oldfelt, V. and Zetterstrom, R. (1959): Acta paediat. (Uppsala), **48**, 1.
6. Kerr, D. N. S., Warrick, C. K. and Hart-Mercer, J. (1962): Clin. Radiol., **13**, 85.