Congenital hepatic fibrosis

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CONGENITAL hepatic fibrosis is an uncommon cause of portal hypertension and usually presents as alimentary bleeding in childhood or adolescence. The occurrence in more than one member of a family has been described (Kerr *et al.*, 1961; Campbell *et al.*, 1958). This report concerns four members of one family who have presented with clinical features attributable to congenital hepatic fibrosis. Patient N.W. was investigated by us and the diagnosis of congenital hepatic fibrosis established. Because of a history of alimentary bleeding in three other members of the family their case records were obtained and studied. The family tree is shown in Fig. 1.

Glasgow Royal Infirmary, for more detailed investigation. She gave a history of intermittent upper abdominal pain culminating in two haematemeses in 1965. Her childhood was healthy. She had miscarriages in 1958, 1959 and 1965. She was given a blood transfusion after her miscarriage in 1959 and the following day she had slight jaundice which persisted for about 10 days. In 1962 she gave birth to a normal full-term child.

Physical examination revealed no significant abnormality. She had no obvious stigmata of liver disease. Kayser-Fleischer rings were not detected. Neither liver nor spleen was palpated. There was no abnormality of the central nervous system.

FIG. 1. Incidence of congenital hepatic fibrosis in a single family.

Case reports

Case 1

The first patient, a female, aged 30, was admitted to Paisley Royal Alexandra Infirmary under the care of Dr S. G. McAlpine following two episodes of haematemesis and was later transferred to the University Department of Medicine,

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Investigations. Barium meal demonstrated changes indicative of oesophageal varices and duodenal ulcer. Intravenous pyelogram was normal. Haemoglobin was 11.3 g with persistent leucopenia and thrombocytopenia. There was no reticulocytosis or increased red cell fragility and bone marrow examination showed normoblastic erythropoiesis.

Representative liver function tests were: serum albumin 3.2 g/100 ml, serum globulin 3.6 g/100 ml, thymol turbidity 1.8 units, alkaline phosphatase 18.0 K.-A. units and bromsulphthalein retention of 15% in 30 min. Coombs' test was negative and no irregular antibodies were found. The half-life of $^{51}\text{chromium}$ -labelled red cells was normal at 26 days and the spleen to liver ratio was 2.4:1. Faecal blood loss was raised at 9 ml daily.

The serum iron was 65 μg /100 ml with a 20% saturation. Serum copper oxidase and caeruloplasmin levels were normal. Activation analysis of blood, hair and nails all gave normal copper levels. A percutaneous needle biopsy of liver showed a normal liver architecture intersected by a thick band of dense acellular fibrous tissue.

The patient was transferred to the care of Professor W. A. Mackey for surgical relief of portal hypertension.

Operation. The spleen was enlarged and numerous varices were seen. Splenic pulp pressure was 36 cm H_2O . A portal venogram showed a dilated but patent portal vein. Splenectomy and spleno-renal anastomosis were done with a fall in splenic vein pressure to 26 cm water. The diagnosis of congenital hepatic fibrosis was confirmed by the surgical biopsy (Fig. 2).

Ten months after operation the serum globulins and alkaline phosphatase remain slightly elevated but the haemoglobin, white cell count and platelet count are normal.

Case 2

The second patient, a female, aged 31 years, underwent laparotomy in Canada in 1964. Dyspeptic symptoms ascribed to a peptic ulcer had been present for several years and these had failed to respond to medical management. There was no history of jaundice. She had no children but had had one miscarriage. At laparotomy she had a chronic ulcer of the first part of the duodenum. In addition, the spleen was enlarged, the liver was decreased in size and the kidneys and adrenal glands were normal. Splenectomy and liver biopsy were undertaken in addition to gastroenterostomy and vagotomy. She died in 1957, aged 34, following massive haemorrhage from oesophageal varices. At necropsy the liver was reported as showing coarse lobulation. The sections of liver have been examined and are typical of congenital hepatic fibrosis (Fig. 3).

Case 3

The third patient, a female, aged 12, complained of abdominal pain in 1933. Jaundice and splenomegaly but no hepatomegaly were noted. The diagnosis of acholuric jaundice was made and splenectomy was undertaken. The liver was observed to be finely granular and cirrhotic at operation. She died 2 weeks after operation from secondary haemorrhage. A section of spleen has been reviewed and shows changes in keeping with portal hypertension. No sections of the liver are available.

FIG. 2. Surgical biopsy of liver. The liver parenchyma is intersected by a thick band dense of fibrous tissue containing numerous small bile ducts; the lobular architecture of the liver is preserved. (H. & E., $\times 42$).

FIG. 3. This section shows a single liver lobule surrounded by dense fibrous tissue. There are three arterial radicles in the fibrous bands unaccompanied by portal veins. (H. & E., $\times 105$).

Case 4

The fourth patient, a male, aged 15, died in 1940 following a massive haematemesis. He had previously had alimentary bleeding and was reported to have 'splenic anaemia'. No post-mortem was done.

Other members of the family

Both the father, aged 68, and mother, aged 69, are alive and well. There is no known consanguinity. Neither has any detectable abnormality of blood and their liver function tests are normal. Both maternal and paternal grandmothers of the patients died in their third decade but the cause of death is not known, though thought to be associated with childbirth. A brother died aged 2, following an intussusception. A sister, aged 40, has four healthy children and has had no miscarriages. As she lives in Canada she could not be examined. Two sisters were not willing to be examined. One aged 35, has no family and has had no miscarriages and the other aged 33 has two healthy children. A fourth sister, aged 28, is said to have had a cerebrovascular accident aged 19, from which she has made a good recovery. She has no hepatosplenomegaly. Haemoglobin, white cell count, platelet count and liver function tests are normal. There is no history of jaundice in any member of the family.

Discussion

The increase in fibrous tissue with lobulation of the liver and increase in bile ducts found in

this condition were discussed by MacMahon in 1929 and 1955. The clinical features have more recently been described (Kerr *et al.*, 1961; Campbell *et al.*, 1958) and the descriptive term of congenital hepatic fibrosis given (Parker, 1956). About fifty cases have probably now been recorded (Hickie & Garvan, 1962). It causes portal hypertension and often presents in infancy as massive alimentary haemorrhage from oesophageal varices. Most patients have been under 16 years of age though older cases have been recorded. There has been a slight female preponderance of cases. Several authors have noted a familial tendency in about one third of cases (Kerr *et al.*, 1961; Campbell *et al.*, 1958) and have felt that generally the disorder is compatible with a recessive mode of inheritance or a dominant mode following mutation. Hickie & Garvan (1962) believe that they have seen the condition in successive generations and suggest a dominant gene with variable penetrance in which the homozygous state causes stillbirth and the degree of clinical severity in the heterozygote is related to the degree of penetrance. Some features of the condition are similar to congenital cystic disease involving liver and kidney, but macroscopic cysts are not found in congenital hepatic fibrosis. The pattern of inheritance is different and portal hypertension, so common a feature of congenital hepatic fibrosis, is rarely, if ever, found in polycystic disease of the liver. Reports have mentioned the frequency of polycystic kidneys in congenital hepatic fibro-

sis, especially in the familial form, but Kerr *et al.* (1962) believe that the commonest renal abnormality, often discovered co-incidentally by histology is 'medullary sponge kidney' with tubular dilatation, especially involving the collecting ducts. Renal function is usually normal in congenital hepatic fibrosis. Macroscopically the liver is usually enlarged and firm and may be lobulated or appear finely 'cirrhotic'. The histology of the lesion, however, is characteristic and has been documented in detail by other authors (Parker, 1956; Kerr, Warrick & Hart-Mercer 1962). The masses of hepatic tissue partially or completely surrounded by fibrous bands have a normal lobular architecture and comprise single lobules or several lobules. The aetiology of the portal hypertension is in doubt; Kerr *et al.* (1961) postulate that portal veins are maldeveloped and that this is the cause of raised portal pressure. A paucity of portal veins was noted in the second case reported here. In the present series the possibility of an epidemic of viral hepatitis in the family was considered. The third patient, however, had died 2 years before the birth of the first patient, making this aetiological possibility unlikely. Moreover, post-hepatic cirrhosis can be distinguished from congenital hepatic fibrosis on histological grounds in that the latter shows an erratic distribution of fibrous bands usually containing an excessive number of small bile ducts, absence of regeneration nodules, and a liver architecture which is essentially normal.

The patients reported here are of interest in that they demonstrate the development of portal hypertension at various ages due to a single cause. The familial cases reported previously have all tended to be children of similar ages (Sweetnam, 1955; Campbell *et al.*, 1958) rather than as described here. The findings of relatively normal liver function tests is usual in congenital hepatic fibrosis, and this in association with a family history, should alert one as to a possible unusual cause of portal hypertension. The treatment is

surgical, usually splenectomy with either a spleno-renal or porta-caval shunt. Results in congenital hepatic fibrosis should be better than in cirrhosis of the liver since liver function is much better preserved (Morales, 1965).

Summary

Four cases of hepatic fibrosis and portal hypertension in one family are described. They belong to one sibship—three sisters and one brother. Histological features of the liver supported the diagnosis of congenital hepatic fibrosis. The family was unusual in that the ages of presentation were different. The patients described illustrate the preservation of hepatic function and the clinical presentation from the effects of portal hypertension suggesting a good result may be anticipated from surgery.

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