Short Reports

The clinical spectrum of chronic liver disease in children presenting to a tertiary level teaching hospital in New Delhi

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TROPICAL DOCTOR 2008; **38**: 101–102
DOI: 10.1258/td.2007.060019

SUMMARY We report on the clinical spectrum of chronic liver disease (CLD) in children presenting to a tertiary level teaching hospital. Children aged <14 years with suspected CLD presenting to the paediatric gastroenterology department of Maulana Azad Medical College between January 1999 and December 2004, were prospectively studied. They were all given liver function tests, abdominal ultrasonography, endoscopy, viral markers and were checked for Wilson's disease, autoimmune hepatitis and liver biopsy wherever feasible. Other tests for metabolic liver diseases were done when indicated. CLD was diagnosed in 174 children over the six-year period. Cryptogenic cirrhosis was the most common entity, followed by hepatitis B-induced liver disease and Wilson's disease. Most patients presented late with evident portal hypertension.

Introduction

Recent advances in the serodiagnosis of hepatotropic viruses have revolutionized the approach to the diagnosis and understanding of chronic liver disease (CLD). Although many papers have been published on liver diseases in adults, very little has been written on liver diseases in children. Most have focused on specific entities, and papers from developing countries show a different pattern than those from the developed countries. Our study aims to define the clinical spectrum of CLD in children presenting to a tertiary level teaching institution in northern India.

Patients and methods

All children attending the paediatric gastroenterology unit at the Maulana Azad Medical College between January 1999 and December 2004 with suspected liver disease were assessed in detail for the cause of liver damage. Investigations included: liver function tests; ultrasonography of the abdomen; upper gastrointestinal endoscopy; liver biopsy (whenever indicated and where feasible, including special staining); serological markers for chronic hepatitis B and C; and workup for Wilson's disease (serum ceruloplasmin, 24-h urinary copper, D penicillamine challenge and Keyser Fleischer ring). Tests for other metabolic liver disease were done whenever indicated. In all patients, who had clinical and biochemical evidence of acute hepatitis, IgM hepatitis A virus and IgM hepatitis E virus antibody and IgM hepatitis B core antibody were tested. Autoimmune markers anti nuclear antibody (ANA), smooth muscle antibody (SMA) and anti-liver kidney microsomal (anti-LKM) 1 were tested using indirect immunofluorescence whenever no other cause of liver disease could be found.

Autoimmune liver disease was diagnosed when one or more of the auto antibodies (ANA, SMA and anti-LKM.1) tested positive (titres for each antibody >1:40). We also applied criteria proposed by the International Autoimmune Hepatitis Group to define autoimmune aetiology in our patients.

Results

A total of 174 children with CLD were studied. The age range was 1.5 months to 14 years. The male to female ratio was 1.2:1 with 95 boys and 79 girls. The most common presenting clinical features were ascitis in 101(58%), jaundice 82 (47%), anorexia 71 (41%), weight loss 50 (29%), peripheral oedema 48 (28%), melaena 43 (25%) and haematemesis 38 (22%). An episode of jaundice in the preceding 6 months was seen in nine (5.2%) and prior to 6 months in 39 (22.4%). Two patients gave a history of recurrent jaundice. Past history of blood transfusion was obtained in 19 (10.9%). Haematemesis in the past was seen in 15 (8.6%) and encephalopathy in four (2.3%). Four (2.3%) mothers had evidence of chronic hepatitis B infection and eight (4.6%) patients had siblings with chronic hepatitis B infection. Five (2.9%) had family members with autoimmune illnesses. Umbilical sepsis in the neonatal period was found in two (1.1%). Physical examination revealed anaemia in 87 (50%), clubbing in 17 (9.8%), palmer erythema in 11 (6.3%), vitamin A deficiency in 25 (14.4%), vitamin D deficiency in seven (4.0%) and vitamin C deficiency in four (2.3%). No patient had spider naevi or testicular atrophy. Liver was not palpable below the costal margin in 44 (25.3%), was <2 cm in 19 (10.9%) and >2 cm enlarged in 111 (63.8%). The surface of the liver was smooth in 126 (72.4%) while nodularity was felt in only four (2.3%). Left lobe enlargement was seen in 70 (40.2%) and splenomegaly was evident in 120 (69.0%).

Biochemical abnormalities at presentation were: raised total serum bilirubin (>0.8 mg%) in 108 (62.1%); raised aspartate aminotransferase (normal value 5–45 U/L) 109 (62.5%); raised alanine aminotransferase 100 (57.5%); prolonged prothrombin time 80 (46.4%) and hyponatraemia 61 (35.5%).

On abdominal ultrasound, coarsened hepatic echo texture was seen in 139 (79.9%) and ultrasound was normal in 34 (19.5%). An associated portal cavernoma was seen in one

Table 1 Causes of liver disease in 174 children

Causes	*Number (%)*
Cryptogenic cirrhosis	112 (64.4)
Chronic hepatitis B	17 (9.8)
Wilson's disease	11 (6.3)
Neonatal hepatitis	7 (4.0)
Budd-Chiari syndrome	7 (4.0)
Auto immune hepatitis	7 (4.0)
Congenital hepatic fibrosis	4 (2.3)
Extra hepatic biliary atresia	2 (1.1)
Non cirrhotic portal fibrosis	2 (1.1)
Fanconi anaemia with hepatitis B	1 (0.6)
Alpha 1-antitrypsin deficiency	1 (0.6)
Chronic hepatitis C	1 (0.6)
Sclerosing cholangitis	1 (0.6)
Valproate-induced CLD	1 (0.6)
Total	174 (100)

CLD, Chronic liver disease

patient. Upper gastrointestinal endoscopy revealed varices in 116 (66.7%) children. Liver biopsy was feasible in 122 (70.1%). The final diagnosis of these 174 children is shown in Table 1. Cytomegalovirus (perinatal infection) was seen in four of the seven (57.1%) children with neonatal hepatitis. Acute viral hepatitis A at presentation was seen in four (2.3%) children. One patient had hepatitis B-associated nephrotic syndrome.

Discussion

CLD is a severe and often rapidly fatal disease in children. The referral pattern, prevalence of the disease, skills of the physician and the availability of appropriate diagnostic facilities influence the aetiological spectrum of CLD. This six-year study comprising 174 children has shown that cryptogenic cirrhosis is the most common entity encountered. The next most common cause was hepatitis B-induced liver disease, followed by Wilson's disease. The male preponderance encountered in this series is a reflection of the referral pattern in general, resulting from sociocultural factors. Some Indian authors have published the profile of CLD in children. Data from these studies show that Indian childhood cirrhosis (ICC) was the most common entity encountered in the earlier reports.[1] Until the early 1980s, ICC was almost synonymous with chronic hepatitis. Due to the diminishing use of copper utensils for boiling milk, it has now become practically non-existent in India and even large teaching hospitals are reporting it very infrequently (<2%).[2] We did not encounter a single case of ICC in this series. Later publications showed the emergence of neonatal hepatitis syndrome as the most common cause.[3] The incidence of neonatal hepatitis syndrome was low in this study (4.02%) due to an increasing awareness and early institution of treatment by neonatologists across the country. The high incidence of cryptogenic cirrhosis may be due to referral to our institution by various smaller hospitals when they could find no cause for liver disease. It is also possible that hitherto unrecognized infective agents or metabolic causes are responsible for this large cryptogenic group.

Wilson's disease emerged as the most frequently diagnosed metabolic liver disease which was due to the availability of the appropriate diagnostic tests. Other metabolic diseases such as galactosaemia, glycogen storage disorders, hereditary fructose intolerance and tyrosinaemia were not seen. Alpha1-antitrypsin deficiency was seen in only one patient.

Hepatitis B-induced CLD was the second most common entity, though the incidence was only 9.7%. An increasing awareness of universal precautions and the introduction of vaccination against hepatitis B in the national programme have contributed to its decline. Chronic hepatitis C was seen in only one (0.5%) case. A previous study[4] showed that hepatitis B and C together constituted 20% of CLD. Studies from other parts of the world have shown a varied incidence. Bortolotti *et al.*[5] in their data on spectrum of childhood chronic hepatitis in northern and southern Italy reported metabolic liver disease in less than 2%, whereas hepatitis B-associated chronic hepatitis was attributed to 92% of children with CLD. Giacchino[6] also reported HBV-induced CLD as the most common cause. HBV preponderance has also been reported from China[7] and Pakistan.[8] However, studies from South Africa[9] show a preponderance of biliary atresia and neonatal hepatitis. In contrast, the most commonly seen aetiologies of chronic hepatitis by paediatricians in northern Europe and USA are autoimmune and cryptogenic hepatitis.[10]

Most children presented late as suggested by the presence of evident portal hypertension in 66.7% cases. Further electrolyte abnormalities were very frequent at presentation. Ultrasound emerged as a good modality for the detection of hepatic echo texture with coarsened echo texture, seen in 79.9% of cases.

To conclude, this study suggests that the incidence of chronic hepatitis B and C is rather low in Indian children. Cryptogenic hepatitis emerged as the most common entity. Most children presented late in the disease and, consequently, had a poor prognosis.

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