WILSON'S DISEASE

(A report of two cases)

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ABSTRACT

Two cases of Wilson's disease are reported. First case presented with fulminant hepatic failure and had a fatal outcome. The second had an insidious onset, neurological manifestations, and is progressing satisfactorily on zinc therapy. Problems in diagnosis and treatment are highlighted.

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KEY WORDS : Wilson's disease; Fulminant hepatic failure; Zinc therapy.

Introduction

Wilson's disease is an autosomal recessive disorder characterised by degenerative changes in the brain, cirrhosis and Kayser - Fleischer rings in the cornea and was first described in 1912 [1]. It results from altered incorporation of copper into hepatic proteins such as ceruloplasmin resulting in diffuse accumulation of copper in the cytosol of hepatocytes and later as liver cells are overloaded, copper is distributed to other tissues to which it is toxic. Its incidence is reported as 1 in 50,000-100,000 [2]. The gene concerned has been located on the chromosome region 13 q 14 [3]. Its presentation can be varied. The emphasis falls on different parts at different times. In children the liver is chiefly involved hence called hepatic form and as years advance, neuropsychiatric changes become increasingly important, so called neurological form [4].

CASE 1

A six and half year old Muslim boy born of a second degree consanguineous marriage was admitted with severe epistaxis and abdominal distension for two days. There was no history of bleeding from any other site, trauma or bowel disturbance. No past history of jaundice, hematemesis, abdominal distension or a bleeding disorder. His scholastic performance was satisfactory. He was the youngest of four sibs, first two were healthy, the third sib had died at 8 years of age following severe epistaxis and mild jaundice with cause not known. Examination

revealed a stuporous child with low grade fever, severe icterus, pedal oedema, a hepatomegaly of 3 cm with a sharp border and smooth surface, and splenomegaly of 3 cm with ascitis but no pallor. Slit lamp examination done once the child's condition improved revealed bilateral KF rings.

On investigation he had hemoglobin of 10.8 gm/dl with total and differential leucocyte counts within normal limits. The total serum bilirubin was 23.0 mg/dl direct - positive, SGOT - 112 IU/L, SGPT 22 IU/L, Alkaline phosphatase 4 KA units/100 ml (28.4 IU/L). Alkaline Phosphatase - total Bilirubin ratio 1.2 and SGOT - SGPT ratio - 5. The prothrombin time was 2 min 9 sec as against 14 sec for the control. The HBsAg was negative. Copper studies could not be carried out due to lack of facilities and patients condition not permitting a move. He was managed conservatively with blood transfusions, antibiotics and bowel wash. D-penicillamine was started in a dose of 250 mg twice a day. Child showed marginal improvement but within a month developed hepatic encephalopathy and succumbed to his illness.

Parents and other sibs had no hepatomegaly or KF rings and their liver function tests were normal. Copper studies for the sibs have been advised.

CASE 2

Fifteen years old Hindu girl born of a 2nd degree consanguineous marriage presented to the OPD with deteriorating school performance and increasing lethargy noted over two years. Three previous sibs had died at six, eight and seven years of age with jaundice and abdominal distension but the cause was not known. The girl gave no history of jaundice, involuntary movements or speech disorder. Examination revealed bilateral Kayser - Fleischer rings but no other abnormality.

On investigation, her liver functions were within normal limits, serum and urinary copper studies carried out in Delhi for the patient and family members were as

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given in Table 1. No KF rings were seen in any other member of the family. She was treated with D-Penicillamine 500 mg twice a day for six months with improvement in her scholastic performance. Presently she is on zinc therapy for the past one year with Cap Zevit (61.8 mg zinc) 1 TDS and has shown no deterioration.

TABLE 1

Serum and Urinary Copper Studies

Patient	Serum Nonceruloplasmin Copper µg/dl	Urinary Copper µg/24h
Case Two	135 (Normal)	87 (Normal)
Father	155 (Normal)	180 (Increased)
Mother	160 (Normal)	105 (Normal)
Younger brother	-	28 (Normal)
Younger sister	-	32 (Normal)

Discussion

In a review of 51 consecutive patients with Wilson's disease the mean age for initial symptoms was 15.5 yrs [5]. Our first case presented with fulminant Wilson's disease at six and a half years. In a case of cirrhosis, the liver usually has an uneven surface. In our patient, the liver was smooth probably due to its hepatitis like presentation. The disease may appear as early as the fourth or fifth year of life as acute or chronic hepatitis and pursue a relentless course to liver failure [6]. Establishing a diagnosis of fulminant Wilson's disease can be difficult specially when facilities for copper studies are not available. A setting of consanguinous marriage, death of a sib with similar ailment and clinical features of hepatocellular failure lead to a high index of suspicion. Bilateral KF rings seen under slit lamp examination confirmed this suspicion. The alkaline phosphatase- total bilirubin ratio was 1.2 and SGOT - SGPT ratio was 5.0. Cut off values of less than 2.0 for the former and greater than 4.0 for the latter are associated with a diagnosis of fulminant hepatic failure caused by Wilson's disease [7]. Tests of copper metabolism, including serum and urinary copper, and serum ceruloplasmin levels may not always be abnormal and facilities for their evaluation may not be available. When available the following abnormalities are of major diagnostic

value in patients with Wilson's disease: Serum ceruloplasmin below 10 mg/dl, tissue copper above 25 mg/100 gm of dry weight of liver and a characteristic lack of incorporation of radio-labelled copper into ceruloplasmin following oral or intravenous administration [8]. KF rings may be missed unless looked for under slit lamp examination.

Though D-penicillamine was started, the child succumbed to his illness. The only effective treatment for fulminant Wilson's disease seems to be liver transplantation [9]. The second case posed no diagnostic dilemma. D-penicillamine the conventionally used copper chelating agent for treatment of Wilson's disease is costly and difficult to procure in smaller cities. Zinc therapy appears to be a reasonable option for the initial [10,11] as well as maintenance therapy in Wilson's disease [12]. Sibling and parent screening for early diagnosis and genetic counselling is a must. Noninvasive screening approaches like KF rings, elevated liver enzymes, elevated urine copper or elevated plasma nonceruloplasmin copper are not adequate to identify all asymptomatic cases of Wilson's disease. Symptom free homozygotes will usually have serum ceruloplasmin below 20 mg/dl and liver biopsy for copper content would reveal values above 25 mg/100 gm dry weight [4]. Recently molecular genetics for sibling screening of affected patients has been described using a probe from the linked retinoblastoma gene [13].

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