

Wilson's Disease in a Saudi Family

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ABSTRACT. A Saudi family with Wilson's disease is presented. One member had symptomatic Wilson's disease leading to liver cirrhosis, portal hypertension, and neuropsychiatric syndrome but absent Kayser-Fleischer rings, while four other siblings had asymptomatic Wilson's disease. The patient with the symptomatic Wilson's disease will be presented and the significance of early detection is discussed. It seems that Wilson's disease may be underdiagnosed in Saudi Arabia.

KEY WORDS: Wilson's disease, Family Screening, D-penicillamine, Saudi Arabia.

Introduction

Wilson's disease is an autosomal recessive inherited disorder of copper metabolism, where accumulation of copper occurs in the body, especially liver, brain, kidneys and cornea^[1]. The gene responsible has been recently mapped to the locus of esterase D on the long arm of chromosome 13^[2]. The clinical picture has been well described in the literature^[3-5]. The prevalence is 30/million, being higher in communities with high rate of intermarriages. Since 1988, when the first seven cases were reported from four Saudi families in Riyadh, Saudi Arabia,^[6] few other cases have been reported from other families,^[7-8] and another Saudi family with five affected siblings will be discussed in this paper. It is, therefore, questionable whether Wilson's disease should be rare in Saudi Arabia especially where a high rate of consanguinity among married couples exists, probably it is under estimated or overlooked.

Case Report

A 14 year old Saudi boy from Al-Qunfuda (West of Saudi Arabia), in fourth grade

of elementary school was admitted in November 1991 to King Abdulaziz Hospital in Jeddah, Saudi Arabia, with gradually increasing abdominal distention and intermittent fever for the past two months. His parents were first cousins and he had six siblings, all looked healthy. One sister died five years earlier at the age of 2 years with acute fever. On examination, he was pale and jaundiced. Temperature was 40°C, Blood Pressure 110/70 mmHg, Pulse 110/minute and regular and Respiratory Rate of 16/minute. He had bilateral gynaecomastia and ankle oedema, no flapping tremors. He had moderate ascites, shrunken liver of 8 cm and splenomegaly of 6 cm below the left costal margin. The cardiovascular, chest, and neurological examinations were unremarkable. Fundi were normal, no Kayser-Fleischer rings were detected (even by slit lamp examination). His WBC was 6,900. Eighty percent neutrophils, hemoglobin 10.4 gm%, platelets 63,000, reticulocyte count was 3%. His liver function tests are shown in Table 1. Corrected calcium for albumin and phos-

TABLE 1. Liver function tests on admission and one year after treatment.

Test	On admission (Nov. 1991)	After 1 year (Dec. 1992)
Plasma proteins g/l (60-80)	64	75
Serum albumin g/l (35-50)	18	43
Bilirubin (total) $\mu\text{m/l}$ (2-17)	65	15
Alkaline phosphatase μl (43-154)	1332	874
Alanine aminotransferase μl (6-53)	31	30
Aspartate aminotransferase μl (7-40)	25	58
Gamma glutamyl transpeptidase μl (5-56)	59	21
Prothrombin time	23/12	14/12
Partial thromboplastin time	53/36	42/36

phate, blood glucose, urea and electrolytes and chest x-ray were normal. Urine, stool and blood cultures were negative. Ascitic tap was suggestive of spontaneous bacterial peritonitis infection and *Escherichia coli* was isolated. Accordingly, he was given a course of antibiotics in addition to diuretics and vitamin K. During his hospitalization, he developed neurological abnormalities. He constantly wore a tense grin, had drooling saliva and developed poor hygiene, he also showed intellectual impairment and deterioration in behavior, being impolite and emotionally labile. He developed pill rolling tremors of the right hand and coarse movements of the right foot which were exaggerated when outstretching the hands and disappeared on movements. His gait was ataxic, but his motor and cerebellar systems were intact. He had no rigidity or dysarthria and his cranial nerves were intact. Superficial sensations were decreased in both legs. Further laboratory investigations showed that schistosoma titre, HBsAg and markers, Antinuclear antibodies, and antimitochondrial

antibodies were all negative. Serum iron and ferritin were normal. Copper studies are shown in Table 2. CT-scan was compatible with liver cirrhosis. Endoscopy revealed grade I oesophageal varices. Liver biopsy could not be done due to abnormal coagulation profile in spite of repeated trials for correction. Electromyography (EMG) showed reduced conduction velocities in both lower limbs compatible with peripheral neuropathy.

TABLE 2. Results of screening of the family.

Case	Symptoms	LFT**	Serum copper 70-140 µg/dl	Ceruloplasmin 15-16 mg/dl	Urine copper /24 hr < 50 µg	Wilson's disease
1. 15y. M	-	Normal	120	25	57	-
2* 14y. M	+	Abnormal	50	9	120	+
3. 8y. M	-	Normal	136	24	39	-
4. 6y. M	-	Normal	77	5	151	+
5. 4y. F	-	Normal	40	5	75	+
6. 2y. M	-	Normal	15	6	Not done	+
7. 6/12. M	-	Normal	20	9	Not done	+

2* Symptomatic Wilson's disease discussed in this paper.

** Liver function test.

He was started on d-penicillamine 250 mg TDS. Initially, he showed neurological deterioration for few weeks, later made slow but progressive recovery. His liver function test improved and neurological signs disappeared, but thrombocytopenia remained due to hypersplenism for which splenectomy was planned. His last liver function tests are shown in Table 1. Screening of his siblings showed results as in Table 2. All the asymptomatic cases were started on d-penicillamine which was well tolerated.

Discussion

Wilson's disease should be suspected in every patient who has liver disease of uncertain etiology. Unless it is first suspected, it may be missed. It is not known why different patients have different presentations.^[9] It is fatal if not treated. The prognosis is better if diagnosed early before the appearance of the neurological symptoms or the development of hepatic failure and if the treatment is given uninterrupted throughout life.^[10] This presented case is interesting in several aspects: In spite of the neurological manifestations and liver cirrhosis, he completely recovered both neurologically and regarding liver function within one year of initiating therapy with d-penicillamine. This underlines the fact that the presence of liver cirrhosis in Wilson's disease patients does not mean a grave prognosis as treatment can increase longevity over that of similar patients with chronic active hepatitis and cirrhosis of different etiologies.^[11]

Liver biopsy could not be performed in this patient as mentioned earlier, due to the prolongation of prothrombin time and low platelets counts, in spite of several trials for correction. It was planned to do liver biopsy while performing splenectomy.

However, the typical presentation, the positive family screening and the favorable response to treatment proved the diagnosis of Wilson's disease.

Another point of interest in this case was the absence of Kayser-Fleischer ring which is present once the nervous system is involved in almost all patients.^[12]

Psychiatric changes due to cerebral cortex involvement can occur as a presenting feature or later in the disease course as in this patient.^[13] Sensory abnormalities are absent in Wilson's disease^[4] due to sparing of the nerve axons. The peripheral neuropathy in this patient was hereditary as four other siblings had abnormal EMGs.

The response to d-penicillamine treatment may be delayed for up to six months and neurological deterioration might occur initially as seen in this patient, which may necessitates the change of treatment to Ammonium Tetrathiomolybdate which is shown to be effective.^[14] Orthotopic liver transplantation remains the definitive treatment and it was entertained initially in this patient when he did not show signs of improvement. It is shown to improve neurological symptoms as well as improving the basic metabolic defect.^[15]

In conclusion, the importance of early detection of this treatable disease in Saudi Arabia should be stressed, where both consanguinity in marriage and chronic liver disease are common. Routine Ceruloplasmin estimation as a screening test in young patients with liver disease may need to be introduced. This screening policy is carried out in Sardinia (Italy) where Wilson's disease is common.^[9]

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مرض ولسون في عائلة سعودية

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المستخلص . تعرض هذه الدراسة لعائلة سعودية ظهر فيها مرض ولسون وقد وجد أن أحد أبناء هذه العائلة مصاب بمرض ولسون العرضي مع تليف في الكبد وارتفاع في ضغط الوريد البابي ومتلازمة النفساني العصبي دون ظهور حلقة كيزر فلايشر . أما الأشقاء الأربعة الآخرون فكانوا مصابين بمرض ولسون اللا أعراضي ، وسوف نتحدث عن المريض المصاب بمرض ولسون العرضي وناقش أهمية الاكتشاف المبكر لهذا المرض ، ويظهر أن هناك نقصاً في تشخيص مرض ولسون في المملكة العربية السعودية .