WILSON'S DISEASE

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INTRODUCTION

Wilson's disease is an autosomal recessive abnormality in the hepatic excretion of copper that results in toxic accumulations of the metal in liver, brain and other organs. The disease occurs in populations of every ethnic and geographical origin and has a word-wide prevalence of about 1 in 30,000 with a carrier frequency of 1 in abnormal gene (the locus on the long arm of chromosome 13) is present in all racial group studied so far and a higher incidence has been noted in Arabs, Chinese, Japanese and Indians.

The metabolic defect in Wilson's disease is an inability to maintain a near zero balance of Copper. Excess copper, small amount of which are essential to life, accumulates possibly because hepatic lysosome lack the normal mechanism to excrete into the bile, the copper that has been catabolically cleavaged from the caeruloplasmin. Since excess copper in vitro inhibits the formation of caeruloplasmin from apocaeruloplasmin and copper is eventually exceeded and released into blood and uptake in extrahepatic sites occur. In 90% of the patients the disease presents with jaundice, hepatic disease or with neurological/psychiatric manifestations.

Symptoms may be diverse and present between the ages of 14 and 40 years. Wilson's disease should be considered in any patient under the age of 40 with an un-explained disorder of CNS, signs and symptoms of hepatitis, chronic active hepatitis, un-explained persistent elevations of serum aminotrans-ferases, hemolytic anaemia in the presence of hepatitis, unexplained cirrhosis, or in any patient who has a near relative with Wilson's disease.

Clinical and Biochemical Profiles

The diagnosis is confirmed in suspected cases by the demonstration of either.

1 A serum concentration of caeruloplasmin less than 200mg/L and Kayser-Fleischer rings (K. Frings) OR

2 A serum caeruloplasmin less than 200 mg/L and a concentration of copper in liver biopsy greater than 250 ug / gram of dry weight.

3 Most symptomatic patients also excrete more than 100ug copper per day in urine and exhibit histologic abnormality on liver biopsy (normally < 40 ug / 24 hours).

4 In about 5% of the patient have a serum concentration of caeruloplasmin greater than 200 ug/L and some patients with

other hepatic disorders chiefly primary biliary cirrhosis, have elevated hepatic copper levels, and, rarely K F rings.

5 In either circumstances, measurement of the ability to incorporate radio-active copper into caeruloplasmin is useful as a discriminating test.

CASE REPORT

In this first family from Peshawar, both mother and father were normal with the only laboratory abnormality was slightly increase urinary copper excretion. Amongst the children two suffered from the disease. Further detail of the family is stated below in table 1.

Another family was from district swat where mother has increase excretion of urinary copper. Amongst the children one son died from the hepatitis at the age 6 the other has neurological presentation with difficulty in walking and had cirrhosis liver as detailed in table 2.

The third family was from District Swat where the mother had increase excretion of urinary copper with the rests of test being normal. One of the child suffered from full blown Wilson's disease with both hepatics and neurological signs and sentences while the younger patient age 4 is asymptomatic with low serum cearuloplasmin level of < 0.174 and increase urinary copper excretion shown below in table 3.

DISCUSSION

Three families were screened and amongst them seven patients were diagnosed as Wilson's disease, as shown in the tables. One died at the age of 9, three

SUMMARY OF THE PATIENTS WITH WILSON'S DISEASES

Name	Age year	Sex	S copper ug/dl	S ceruloplasmin G/L	Urinary copper ug/day	K F rings
Father	45	M	70.6	0.316 N	120.3	Absent
Mother	40	F	80.4	0.386 N	40.2	Absent
FK	14	F	49.3	<0.0972	154.5	Present
LM	12	F	35.7	<0.097	394.5	Present
KM	9	M	119.1	<0.166	45.5	Absent
NM	7	M	83.6	0.243	42.6	Absent

TABLE – 1

SUMMARY OF THE FAMILY WITH WILSON'S DISEASE

Name	Age years	Sex	S copper ug/dl	S ceruloplasmin G/L	Urinary copper Ug/day	K F rings
Father	36	M	38.2	0.402	28.6	Absent
Mother	30	F	42.6	0.382	134.5	Absent
IJ	9	M	108.4	<0.097	265.5	Present
	6	M	–	–	–	–

TABLE – 2

SUMMARY OF THE PATIENTS WITH WILSON'S DISEASE

Name	Age years	Sex	S copper ug/dl	S ceruloplasmin G/L	Urinary copper Ug/day	K F rings
Father	45	M	42.2	0.364	125.5	Absent
Mother	38	F	34.8	0.412	50.0	Absent
NA	14	F	156.7	<0.0834	363.5	Present
AK	11	F	36.0	0.316	43.5	Absent
AA	8	M	40.0	0.422	46.5	Absent
JB	4	F	132.4	<0.174	186.5	Absent

TABLE – 3

presented with jaundice, hepatitis and chronic active hepatitis while the rest of the three presented with neurological manifestations.

Wilson's disease tends to preset as liver disease in adolescents and neuropsychiatric disease in young adults. But there is great variability. The diagnosis should always be considered in any child or young adult with hepatitis splenomegaly with hyperplenism, hemolytic anemia, portal hypertension ,and neurologic or psychiatric abnormalities. Wilson's disease should also be considered in persons under 40 years of age with chronic or fulminant hepatitis of uncertain cause. Sometime it may be missed easily in a reagon with endemic problems. A review of 25 cases in Brazile[1] which was thought to have schistosomiasis proved to be Wilson's disease[6], Four cases had neurological presentation with the rest suffered from hepatic cirrhosis. 15% of them were found to Kayser Fleischer ring.

Hepatic involvement may range from elevated liver tests to cirrhosis and portal hypertension. The neurologic manifestation are related to basal ganglia dysfunction and include a resting, postural, or kinetic tremor and dystonia of the bulbar musculature with resulting dysarthria and dysphagia. Psychiatric feature include behavior and personalty[2] changes and emotional liability. The pathognomonic sign of the condition is the brownish or gray green Kayser –Fleischer ring. RT Gower et al,[3] reviewed 30 cases over a period of three decade, 22 of them had liver problem (with 8 fulminant failure and 14 had chronic liver disease), 3 with neurological presentation, 1 had haemolysis and 4 were asymptomatic siblings of the patients with Wilson's disease. 70% of them were diagnosed within 6 months of the suggesting symptoms and signs, 18 % had Kayser Fleischer ring. All had increased liver copper levels except 1 and had 6 years successful treatment with penicillamine with good response.

The diagnosis can be challenging and is based on demonstration of increase urinary copper excretion (>100mg/24h) or low serum ceruloplasmin levels (<20mg/dl), and elevated hepatic copper concentration (>250 mg/g of dry liver). In equivocal cases the diagnosis may require demonstration of low radio labeled copper in corporation in to ceruloplasmin.[4]

Screening of the family members is essential part of any patient with Wilson's disease. And screening of children should be after thee years of age.

Women with cirrhosis due to copper toxicity have an increased risk of infertility, abortion and premature delivery. Because of the teratogenisity with penicilliamine, pregnant patients are treated with zinc.[5,6]

Early treatment[7,8] to remove excess copper (with penicillamine) is essential before it can produce neurologic or hepatic damage. Prognosis is best in the asymptomatic individuals who are detected early, by screening the families.

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