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A CASE REPORT OF WILSON'S DISEASE

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ABSTRACT

Wilson's disease is due to impairment in the ability of liver to incorporate copper into hepatic ceruloplasmin and to export copper from the liver into bile. This is due to the defective transport of copper by the copper-transporting P-type ATPase secondary to one of several mutations in the ATP7B gene 2519. We conclude that Wilson's disease is not uncommon in our local population; possibly poor recognition is the cause of it's under and delayed diagnosis. Wilson's disease can present in children with isolated neuropsychiatric features without any hepatic manifestation. All young patients, below the age of 40 years, presenting with neurological or psychiatric features as initial manifestations should be thoroughly screened for Wilson's disease.

KEYWORDS: Wilson's disease, Ceruloplasmin, Copper, Kayser-Fleischer (Kf) ring.

INTRODUCTION

Wilson's disease (WD) was first identified by Kinnear Wilson in 1912. The incidence of the disease is reported as 1/30000- 1/100000 births.[1] Wilson's disease is due to impairment in the ability of liver to incorporate copper into hepatic ceruloplasmin and to export copper from the liver into bile. This is due to the defective transport of copper by the copper-transporting P-type ATPase secondary to one of several mutations in the ATP7B gene 2519.[2]

Diagnosis solely based on clinical manifestations and biochemical parameters lacks accuracy. Copper is an essential trace element in the human body and a required component of many proteins. Excess copper causes oxidative damage to hepatocytes and allows spillage of free

copper into the blood. It will overload other organs such as the brain, kidney and cornea, initiating toxic damage.[3]

However, excessive cellular copper damages neuronal and metabolic functions, which is displayed by the wide spectrum of symptoms in WD. The defective gene, ATP7B, is responsible for this disorder.[4] It is of 2 types according to the age of onset. Hepatic form is more common in form in adults. The prevalence of WD in Asian countries varied between 33 and 68 per 10,000 in the early 2000s which is a bit more than in European population varying between12 and 29.[5]

Clinical manifestations of WD include neurological symptoms such as dystonia, tromor, dysarthria, psychological disturbances. It also includes hepatic diseases like liver disease/ cirrhosis, renal tubular dysfunction, hypercalciuria, hyperphosphaturia, hypokalemia, gyneco-logical abnormalities, cardiovascular dysfunction can be seen in WD.[6]

The medical treatment of Wilson disease's patients can be based on the use of chelating agents. These are capable of raising blood copper concentration and its renal excretion and this could explain why some patients may experience worsening of symptoms in the beginning of treatment. Zinc treatment has been indicated ideally for medical treatment for individuals.[7]

MEDICAL TREATMENT RECOMMENDATIONS IN WILSON'S DISEASE.[8]

• Treatment recommendations for Wilson's disease are in transition. There is increasing confidence in the use of trientine rather than penicillamine for initial chelation therapy of neurological and hepatic disease.

• Zinc alone has been advocated for pre-symptomatic and asymptomatic Wilson's disease, although some clinicians still prefer a chelator. For maintenance therapy, reduced dose of chelator or replacement with zinc alone are options.

Dimercaprol (BAL) is the first drug to be introduced in the treatment of WD in India. Penicillamine is the most commonly used de-coppering drug globally, but there is no comprehensive documentation of its use in clinical practice in the Asian populations. A few cases exhibit paradoxical worsening in India. Some of the rare adverse events like Steven Johnson syndrome, myasthenia gravis and pseudoxanthoma elasticum have been reported. Trientine was introduced as an alternative to penicillamine in 1969 and has few side effects. It is an effective treatment for WD and indicated penicillamine.[9]

CASE PRESENTATION

A 30years old female was admitted in General Medicine department with the chief complaints of decreased appetite since 1 month and loss of weight. Past history was found to be haemorrhoidal bleeding for 2 months. Patient was known case of hypothyroidism since 15 years and on medication (Tab. Thyronorm 100µg).

GENERAL EXAMINATION

On examination patient was found to be Pallor^{++}, pedal oedema^{+}, with increased jugular venous pressure, Pulse rate: 100/min. Lungs were clear, Par abdomen showed Ascites & mild splenomegaly.

LABORATORY INVESTIGATIONS

Complete blood picture: Haemoglobin 5gms%, Packed cell volume: 14 vol%, Reticulocyte count: 3%, RBC: 1.8million cells, Mean cell volume: 70FL, Mean cell haemoglobin: 20.5pg, Mean cell haemoglobin concentration: 24.9g/dl. White blood cells were found to be normal. Finally RBC smear revealed an impression of predominantly microcytic, hypochromic; tear drop cells+, few ovalocytes.

Ultra sounds scan of abdomen revealed an impression of coarse echo texture of liver (chronic liver disease), Splenomegaly, Ascites. Serum electrolytes, random blood sugar, renal and liver functional tests were found to be normal.

DIFFERENTIAL DIAGNOSIS

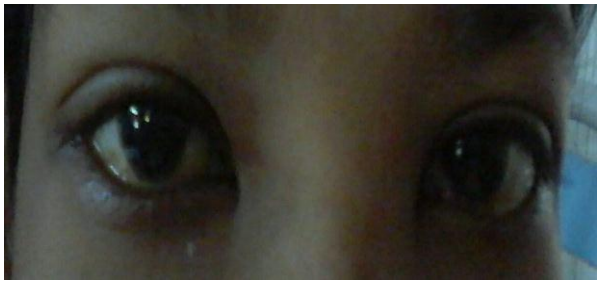
Anti nuclear antibodies (ANA) revealed an impression of positive for ANA. 24 hours urine copper was found to be much higher 433µg/day. Direct coomb's test: Negative and Ceruloplasmin levels were found to be 12.60mg/dL. Ophthalmology eye report revealed mild copper ring in the eye was positive.

Based on the above complaints and lab data, condition was finally confirmed as **WILSON DISEASE's** WITH HYPOTHYROIDISM.

TREATMENT

Initially symptomatic treatment was started based on complaints and history of the patient, which follows Tab. Iron folic acid TID, Tab.Pantoprazole 40mg OD, one packed blood transfusion was given for 2 days. Then Inj.Furosemide 20mg IV BD, Inj.Ondansetron 4mg IV BD, Inj.Metronidazole 100ml IV TID continued for 10 days with adding Tab. Zinc acetate

50mg BD, T.Ciplar LA 60mg OD and Tab. Thyronorm 50µg OD on day six. Finally the patient was discharged with the following medications, Cap.Dexorange TID, Tab.Ascazin 50mg BD, Tab.Thyronorm 50µg OD, Tab.Dytorplus OD. Tab.Pantoprazole 40mg OD. By recommending low salt diet.



Picture no: 1 Denotes mild kf ring in the right eye

DISCUSSION

Table 1: Copper evaluation in healthy subject and patient with wilson's disease.[9]

Parameter	Healthy patients	Wilson's disease	In this case
Ceruloplasmin in plasma	0.2-0.4g/l	<0.1g/l (normal in 10% of patients with wilson's disease)	Positive
Serum copper	13-22µmol/l or 0.8-1.4mg/l	<10µmol/l or <0.6mg/l can be normal if acute hepatitis or haemolysis	Positive
Urinary copper	<0.8µmol/24h or <0.05 mg/24h	>1.5µmol/24h or 0.096 mg/24h	Not done
Copper in liver	<0.9µmol/g of dry tissue or >56µg/g of dry tissue	>4µmol/g of dry tissue or >250µg/g of dry tissue	Not done

The 24-hour urinary copper measurement may be the single best screening test for Wilson's disease, especially in individuals with neurological or psychiatric dysfunction. Urinary copper levels in symptomatic Wilson's disease patients typically exceed 100 mg/d. They may also be elevated in several liver disorders. This distinguishing between diseases is important during diagnosis.[10]

Which was actually same confirmed in this case, which matches with above criteria.

CONCLUSION

We conclude that Wilson's disease is not uncommon in our local population; possibly poor recognition is the cause of it's under and delayed diagnosis. Wilson's disease can present in children with isolated neuropsychiatric features without any hepatic manifestation. KF rings along with neuropsychiatric features and a low Ceruloplasmin level are sufficient to establish a diagnosis of Wilson's disease. Low Serum Ceruloplasmin (< 20 mg/dl) is more reliable in

supporting the diagnosis of Wilson's disease than 24 hour urinary copper excretion and low serum copper levels.

All young patients, below the age of 40 years, presenting with neurological or psychiatric features as initial manifestations should be thoroughly screened for Wilson's disease.

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