Bangladesh Medical Journal 2010, 39(2)

Case Report

Case Report on WILSON'S DISEASE: An Unusual Presentation

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Abstract

A 55 years old lady born of non-consanguineous parents, mother of four healthy children presented with recurrent episods of alterted consciousnes for the last 2 years. Clinically the patient was diagnosed as a case of chronic liver disease with complications. Biochemical Investigations confirmed the diagnosis of WILSON'S DISEASE which is very rare above the age of 40.

Key words: WILSON'S DISEASE, Neuropsychiatric disorder, ceruloplasmin, Penicillamine, Zinc acetate

Introduction

Wilson's disease is autosomal recessive disorder of copper metabolism. First described in 1912, it is caused by at least 200 different mutations in gene ATP7B on chromosome 13 resulting in deficiency of ATP7B protein. It is almost always associated with failure of synthesis of ceruloplasmin, ultimately impairing biliary copper excretion resulting in positive copper balance, hepatic copper accumulation and copper toxicity from oxidant damage. The organs mostly affected are liver, basal ganglia of brain, eyes, kidney and skeleton. Hepatic disease occurs predominantly in childhood and adolescence, although it can present in adults in their fifties. It manifests in the form of acute hepatitis, cirrhosis or as hepatic decompensation which is associated with jaundice, hypoalbuminaemia, coagulopathy, ascites, peripheral edema, hapatic encephalopathy and if severe, haemolytic anaemia. Neurologic manifestations typically occur in patients in their early twenties, although age of onset may extend into sixth decade of life. Basal ganglia is the region most commonly involved but occasionally pons, medulla, thalamus, cerebellum and subcortical area may be involved. Movement disorders including dystonia, incoordination, tremor and choreoathetosis are common as are dysarthria, dysphagia and features of Parkinsonism, memory loss, decreased IQ, features of dementia, migraine type headache, seizure and autonomic disturbances may also occur.

Psychiatric disturbances include emotional lability, depression, mania, personality change, delusion and loss of sexual inhibition. Kayser Fleischer (KF) rings are present in the junction of cornea and sclera in >99% of patient with neuropsychiatric form of disease and have been described very rarely in the absence of Wilson's disease. Renal tubular damage causing haematuria and osteoporosis with osteoarthritis, particularly of knee may occur, but are virtually never presenting features.

Serum ceruloplasmin level though useful, should not be used alone for definitive diagnosis, because they can be normal in up to 10% of affected patients and decreased in 20% carriers of mutant gene of Wilson's disease and also in advanced liver failure from any cause. Absence of KF ring does not exclude the diagnosis, but presence pretty much ensures it. Urinary copper level is >100 µg/ 24 hr in symptomatic patients but may be in range of 60 to 100 µg/ 24 hr. The gold standard for diagnosis remains liver biopsy with quantitative copper assay. Affected patients have values > 3.1 µmol/g or > 200 µg/ g of dry weight of liver. Copper stain is not reliable Genetic testing by mutation screening for diagnosis is not yet practical simply because of number of mutations (>200).

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Case Report

A 55 years old lady, born of non-consanguineous parents, mother of four healthy children, presented with recurrent episodes of altered consciousness for the last 2 years. The episodes started with the patient being lethargic and irritable and gradually she became mute and stuporous. The patient has suffered from 10-12 episodes weithin the period of two years, each episode lasting for 4-5 days on average with spontaneous partial recovery. Patient's family members started to notice that she was depressed, inattentive and clumsy in her daily activities and forgetful even in between the attacks. On psychiatric consultation, she was diagnosed as a case of somatoform disorder and was treated with antipsychotic with no improvement. She also suffered from pain and swelling of multiple joints for the last 12 years, more prominent in the wrist, elbow, knee and finger joints bilaterally. She was'treated as a patient of Rheumatoid arthritis with methotrexate for 6 months, steroid for 1 year and NSAIDs for longtime within this period. Patient complained of occasional low grade fever, abdominal pain, constipation, nausea and vomiting with an episode of vomiting of blood. She also narrated that her joint problems improved subsequently, but as her neurological condition deteriorated gradually, she was admitted to medicine unit of DMCH through emergency department.

On admission, the patient had altered consciousness with GCS score of 9/15, she was mildly anaemic, moderately icteric with bilateral dependent edema, moderate ascites and just palpable spleen. Her plantar response was bilaterally extensor. She was diagnosed as a patient of hepatic encephalopathy and after 2 days of supportive treatment, the patient became fully conscious and GCS score improved to 15, plantar response reverted to bilaterally flexor. On subsequent examination, rigidity and resting tremor was found. Slit-lamp examination revealed Kayser fleischer rings in both cornea. Z-deformity of thumb and swan neck deformity of index finger was noticed in both hands.

Laboratory findings- complete blood count revealed Hb level 7.7 gm/dl, total platelet count - 90,000/cmm, ESR- 27 mm in 1 hour. Urine examination, blood urea, serum creatininc, random blood glucose reports were normal. Liver function tests showed serum bilirubin- 5 mg/dl, serum transaminases and alkaline phosphatase normal, prothrormbin time 30 seconds. INR-2.55, serum albumin- 1.8 gm/dl, albumin : globulin ratio- 0.54:1. Serum electrolytes examination showed serum potassium 2.1 mmol/l. USG of whole abdomen- small coarse liver with ascites and mild splenomegaly. Ascitic fluid study showed protein- 1.1 gm/dl, cell count 60/mm3, lymphocytes- 80%, no bacteria found in Grain staining and AFB staining, no malignant cell found. Endoscopy of upper GIT revealed esophageal varices grade-II with fundal and cardial varices, mild portal hypertensive gastropathy and erosive antral gastritis. MRI of brain- mild age related degenerative atrophy of brain, EEG was abnormal with background rhythm showing delta waves bat no epileptiform activity was shown. All these investigations confirmed the presence of CLD with complications. To ensure the diagnosis of Wilson's disease and exclude other possibilities, following investigations were done HBsAg- negative, Anti-HCV- negative, Anti-HEV IgM- negative and ELISA for ANA negative. Serum ceruloplasmin level- 156u (280-570u). Urinary copper concentration 30µg/L and 24 hour urinary output 1.8 liter (refcrence level <40 ig/24 hour).

Treatment: after initial treatment in the form of lactulose, oral potassium syrup, fresh blood and fresh plasma transfusion and maintaining adequate nutrition, her condition improved. It was evidenced by laboratory results - complete blood count - Hb rising up to 9.8 gm/dl, platelet count increasing to l,40,000/cmm, ESR coming down to 10 mm in 1st hour, serum potassium level recovered to 4.2mmol/l. When the diagnosis of Wilson's disease was confirmed, she was given penicillamine 1.5gm/day. After a few days of treatment, her condition further improved. Serum bilirubin decreased to level of 3.9 gm/dl, prothrombin time-24 seconds, INR-2.02. But a few days later, patient again started to become drowsy. Penicillamine was stpopped and treatment with zinc acetate was started. Since then patient is showing signs of clinical improvement and no further attack of altered consciousness was observed.

Discussion

WILSON'S DISEASE though rare but now is often thought as a potential differential diagnosis in a patient of liver disease under the age of 40

without any obvious cause and neuropsychiatric manifestations usually in the form of akinetie-rigid syndrome with or without dyskinesia. Though the signs of liver disease usually manifest in children and neuropsychiatric features in young adult, in this case both the features have started late- after the age of 50 years. The eaiiy signs are slight change in personality, emotional lability or mood change, clumsiness or slowness to solve problems of daily life which are often ignored specially in women in the socioeconomic perspective of our country and leads to needless misery. The fact that the neurological damage is less reversible makes the situation more painful. This case had also an unusual mode of presentation of repeated bouts of altered consciousness and the presence of another disease entity in the form of rheumatoid arthritis with its obvious deformity made the diagnosis doubly difficult. The patient had been previously admitted to medicine unit, DMCH with the same complaints, but after establishing the diagnosis of rheumatoid arthritis, jaundice was probably thought to have occurred as a side effect of methotrexate which she used to receive from before and no further enquiry was done to find out any other cause of jaundice. Her neurological symptoms were labeled as somatoform disorder, perhaps again due to the unusual presentation and antipsychotic medications were given without any effect. Indeed, this is also a worldwide scenario with the half of the patients undergoing psychiatric hospitalization before Wilson's disease is recognized. Up to one-fifth of the patients with Wilson's disease present initially with psychiatric features in isolation, one third with predominantly psychiatric features and two third of the patients of WILSON'S DISEASE eventually develop psychiatric features. Moreover, the psychiatric features may precede neurological signs in early stage of WILSON'S DISEASE.

The scope of investigations are still limited in our country since the facilities of measuring serum copper level or genetic testing are absent. Liver biopsy may be contraindicated in the presence of decompensated liver disease with coagulopathy. It can make the definitive diagnosis of Wilson's disease difficult as serum ceruloplasmin level should not be used alone due to the causes mentioned before. Finally, in this case, treatment with penieillamine was not associated with the improvements expected rather it caused paradoxical deterioralion of neurological signs as expressed in various journals. Zinc acetate may be a suitable alternative as it has few side effects and is affordable to mass population of our couutry.

Conclusion

If any patient present with liver dysfunction ranging from jaundice to hepatic encephalopathy or neurological features in the form of simple mood disorder to Parkinsonism or dementia, the diagnosis of WILSON'S DISEASE should be kept in mind irrespective of age of the individual. Early diagnosis and interdisciplinary approach with good collaboration among medicine specialists, hepatologists, neurologists, and psychiatrists is crucial.

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