CASE REPORT

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MRI Changes in the Brain: A Key to the Diagnosis of Wilson's Disease

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Abstract

A 10 year old boy was presented with weakness of upper and lower limbs and generalized body aches for the last three months. Later he developed mild uncoordinated movements, ataxia, slurred speech and dysarthria. MRI of the brain was advised that showed bilateral T2W hyperintensity in caudate, lentiform nuclei and pons. Ophthalmological examination showed Kayser Fleisher rings. 24 h urinary copper levels established the diagnosis of Wilson's disease.

Key words: MRI changes, Brain; Diagnosis; Wilson's disease.

INTRODUCTION

Wilson's disease (WD) also called 'hepatolenticular degeneration' is an autosomal recessive hereditary disease, that localize to chromosome 13 and is characterized by a deficiency of ceruloplasmin, the serum transport protein for copper. The most pronounced involvement is in the liver, brain, with typical involvement of the lenticular nucleus. Hepatic problems like acute hepatitis, chronic hepatitis, cirrhosis of liver and acute fulminant hepatic failure can occur in early childhood.[1]

It was first described in 1912 by Kinnear Wilson as "progressive lenticular degeneration," a lethal neurologic disease accompanied by chronic liver disease leading to cirrhosis.[2] The gene, ATP7B, also referred to as "WND," encodes a metal transporting P-type ATPase, which is expressed mainly in hepatocytes and functions in the transmembrane transport of copper. Any error in function of ATP7B protein leads to decreased hepatocellular excretion of copper into bile which results in hepatic copper accumulation and hepatocytes injury. Eventually excess copper is released into the bloodstream and deposited in various other organs, notably the brain, kidneys, and cornea. An additional consequence of the loss of functional ATP7B protein is failure to incorporate copper into ceruloplasmin. The hepatic production and secretion of the ceruloplasmin protein without copper results in the decreased blood level of ceruloplasmin found in most patients with WD to the reduced half-life of this apoprotein.[3]

The clinical presentations of WD are hepatic and neuropsychiatric problems. Chronic active hepatitis and cirrhosis are the most common hepatic presentation, but some patients present with fulminant liver failure. Typical neurological sign include tremor, rigidity, drooling, speech changes, and incoordination, unable to perform fine motor tasks, and gait difficulties. Psychiatric manifestations include compulsive and impulsive behavior, aggression, depression and phobias. Average age of clinical presentation of WD is between 5 to 50 years. Early childhood manifestations of WD are chronic liver disease or hemolytic anemia while neurological manifestations are rare before the age of ten years.[4] WD occurs worldwide with an average prevalence of 30 affected individuals per million populations.[5]

Diagnosis is based on clinical evaluation along with biochemical and Neuroimaging confirmation. Biochemical studies reveal a low serum ceruloplasmin level (<20 mg/ dl) and increased urinary copper excretion (more than >100 ìg copper per 24 h). Most definitive method of diagnosis is hepatic copper levels, of more than 250 g/g of dry tissue (Normal 15-55 ìg/g).[5,6] Patients suffering from WD show neuroimaging abnormalities in gray matter of lentiform, caudate and thalamic nuclei.[6] MRI is the investigation of choice providing more elaborate anatomical information than CT scan of brain on the structure of basal ganglia and brain stem. On MRI, abnormal signals are hypointense on T1-weigthed images and hyperintense on T2-weigthed sequences. The high signal intensity on T2 weighted images is believed to be due to edema, gliosis, necrosis and cystic degeneration.[7] The disease is treated with lifelong use of chelating agents such as D-penicillamine or trientine hydrochloride, drugs that help remove copper from tissue and use of zinc for maintenance therapy and for the treatment of asymptomatic sibs.[8,9]

Case Report

A 12 years old boy, born to non-consanguineous parents presented involuntary limb movement and generalized body aches since 3 month. No h/o fever, jaundice, hematemesis, melena, hemoptysis, blood transfusions in the past, rash, joint pains, chest pain, drug intake, bleeding disorders were documented in the family. His developmental milestones were normal. On examination his vital signs were stable. Neurological examination showed dystonia, mild discoordinated movement, exaggerated deep tendon reflexes and ankle clonus was present. Babinski's sign was positive. He was advised EMG which revealed myopathy.

Complete blood count revealed hemoglobin concentration of 11.4 gm/dl. The white blood cell count was 5.2 x 10^9/L (Neutrophil 53%, Lymphocytes

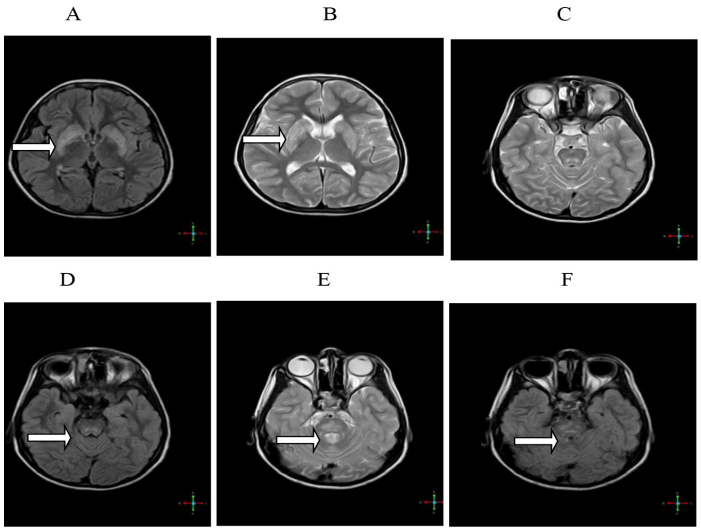

Figure 1: MR images of the brain. (A, B) FLAIR and T2W images shows bilateral caudate and lentiform nuclei hyperintensities. (C, D, E and F) shows bilateral hyperintensities in Pons.

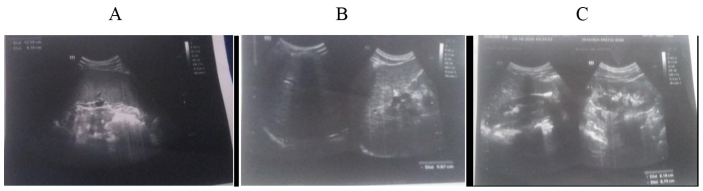

Figure 2: (A, B, C) Ultrasound images show splenomegaly, mild echotexture liver and normal kidneys.

41%, Eosinophils 3%) and platelets count was 175 × 10^9/L. ESR was raised measuring 12 mm at 1st h (Westergren). Liver function tests were normal. Serum Ceruloplasmin level was 10mg/dl (normal 19-57md/dl). 24 h urinary copper was 2.3/24h (normal ≤1μmol/24h). Serum calcium and phosphate levels were 10 mg/dl.

On MRI, T2-weighted images revealed abnormal signal intensities in the bilateral basal ganglia (Figure 1) and pons (Figure 2), appearing hyper intense on T2WS and FLAIR sequences, hypo intense on T1WS. Ultrasound abdomen showed mild coarse echotexture of liver and enlarged spleen measuring 13.5 × 6.3 cm.

Ophthalmoscopic examination by slit lamp showed Kayser-Fleischer rings in both eyes. In our case neurological manifestation was the presenting feature without any association of hepatic involvement detected clinically and by liver function studies.

DISCUSSION

WD is a rare autosomal recessive disorder causing copper overload. Most recent cases have been reported in developed countries.[10] Children with WD are usually normal at birth, may remain healthy and asymptomatic for a variable period of time; most cases may present in the second and third decade of life.[10] The neurological features of WD primarily due to the deposition of copper in the lenticular nuclei, although other areas like the brainstem and cerebellum can also be affected. The long-term treatment of symptomatic cases of WD entails the lifelong use of copper chelators and zinc, while liver transplantation provides a cure. The copper chelators commonly used for WD are penicillamine and trientine hydrochloride.

CONCLUSION

Therefore, it is concluded that neurological features may be the presenting manifestation of WD even in the absence of clinical and laboratory evidence of hepatic involvement. MRI is the modality of choice for the neurologic manifestations. We have described WD in a 10 year old child and highlighted the clinical manifestations of the disease.

ABBREVIATIONS USED

MRI: Magnetic Resonance Imaging; **ATP7B:** Wilson's disease gene; **ATPase:** Adenosine Triphosphatase; **WD:** Wilson disease; **CT:** Computed Tomography; **EMG:** Electromyography; **ESR:** Erythrocyte sedimentation rate.

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