Case Report

Neuro Wilson disease in an adolescent girl – early presentation- a case report

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Abstract

Wilson disease (WD) is an inborn error of copper metabolism caused by a mutation to the copper-transporting gene *ATP7B*. The disease has an autosomal recessive mode of inheritance, and is characterized by excessive copper deposition, predominantly in the liver, cornea, kidney and brain. There are varied clinical presentations for WD. The prognosis depends on various factors like age, sex, organ involvement, time of diagnosis, early initiation of de-coppering therapy and extent of involvement in case of neurowilson disease. In WD excessive copper accumulates in liver then gets redistributed to nervous system, cornea, kidneys and other organs. In first decade of life, hepatic involvement predominates but neurological manifestations occur in third or fourth decade. Studies showed Indian children with neurowilson disease present with behavior abnormality, speech and cognitive impairment, sub-clinical affection of visual pathway and autonomic function.

Here we present a 12 years old girl with primary neurological manifestation of Wilson disease. She presented with abnormal gait, dysarthria and inappropriate laughter. On examination she also had Kayser- Fleischer (KF) ring in both eyes and MRI revealed extensive gray and white matter abnormalities, which suggest poor prognosis in the index case. In spite of good compliance with de-coppering therapy with D- penicillamine and zinc, she had progressive neurological deterioration in the form of progressive dystonia, dysarthria and difficulty in walking.

Keywords: Wilson disease, Autosomal recessive, white matter, KF ring, D-Penicillamine, Zinc

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Introduction

Wilson disease (hepatolenticular degeneration) is an autosomal recessive disorder, which is associated with degenerative changes in the brain, liver and cornea. 1 in 30,000 to 1 in 50,000 births are affected worldwide [1]. Genetic basis is traced to the ATP-7B gene locus on long arm of Chromosome 13 which is critical for biliary copper excretion and for copper incorporation into ceruloplasmin.

Absence or malfunction of ATP7B results in decreased biliary copper excretion and diffuse accumulation of copper in the cytosol of hepatocytes [2]. Normally, copper loss occurs through bile and into faeces. In Wilson disease biliary excretion of copper is impaired and body copper progressively increases, especially in the liver, brain, kidneys and cornea. The serum ceruloplasmin is low and excessive copper exists in the plasma and urine [2, 3].

The excess copper leads to tissue injury and if not effectively treated, may lead to death [2, 3]. Besides the better known basal ganglia lesions, extensive grey matter and even white matter lesions may occur, though much less frequently [4,5]. Index patient is a case of Wilsons Disease with extensive grey and white matter abnormalities and briefly discuss the relevant literature.

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Case Report

A 12 years old girl, born to non consanguineous parents presented with inappropriate smile, involuntary movements of upper limbs, heel walking and progressive dysarthria for the past one year. There was no history seizures, jaundice, bleeding diathesis, fever with rash, joint pain, drug intake or any bleeding disorders in the family.

Her developmental milestones were normal and she was studying 7th standard with average school performance. On examination her vitals were stable. Liver was not palpable. KF ring was present on both eyes. Neurological examination showed dystonia, choreiform movements of limbs, brisk deep tendon reflexes with heel walking. Blood investigations revealed Hemoglobin 11.2gm/dl, WBC count-4300 (neutrophils -63 % & lymphocytes-37%), platelet 1.2 lakhs/. Liver function test was normal. Serum ceruloplasmin levels-8.4mg/dl and urinary copper was 321.76 mcg/24hours and oral D-Pencillamine challenge test showed copper excretion of 1876mcg/24hours. Ophthalmoscopic examination by slit lamp confirmed KF ring in the eyes.

With the clinical diagnosis of Wilson disease, MRI study of the brain was done to know the extent of involvement, which showed T2/FLAIR hyper intense signal in bilateral basal ganglia (caudate nuclei, putamen, part of globus pallidi), thalami, midbrain and bilateral superior cerebellar peduncles (Figures 1 & 2). In addition diffuse T2/FLAIR hyper intensities seen in cortical gray matter and subcortical white matter of bilateral high frontal lobes with evidence of diffuse restriction and mild cerebral atrophy (Figure 3). Patient was diagnosed as Wilson disease and started on D-Penicillamine and zinc therapy. In spite of good compliance with de-coppering therapy with D- Penicillamine and zinc, she had progressive neurological deterioration in the form of progressive dystonia, dysarthria and difficulty in walking.

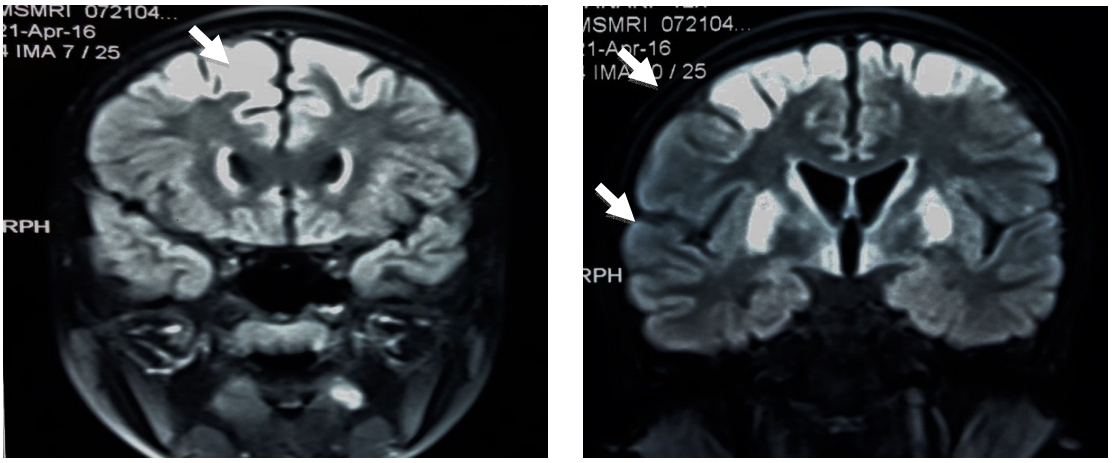
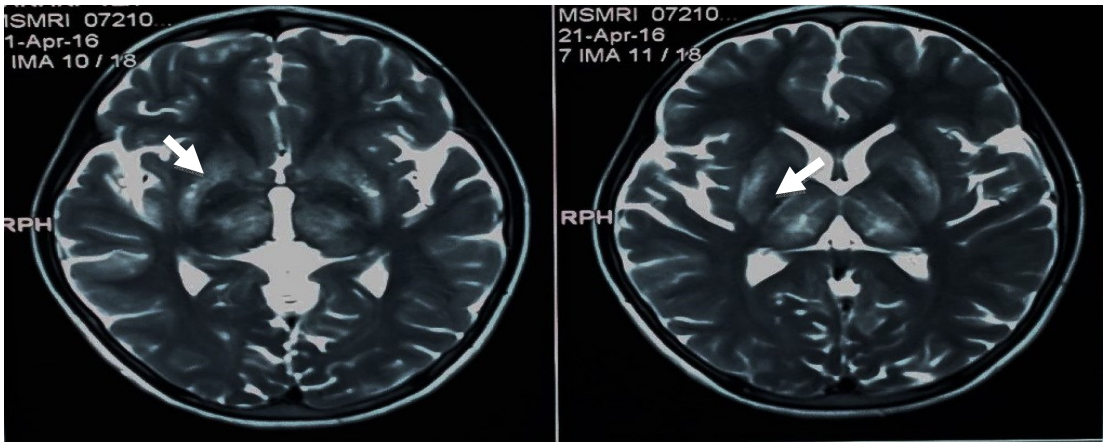


Figure-1: T2 FLAIR coronal images showing hyper intense signal (arrows) in cortical gray matter and subcortical white matter of bilateral frontal lobes and basal ganglia.



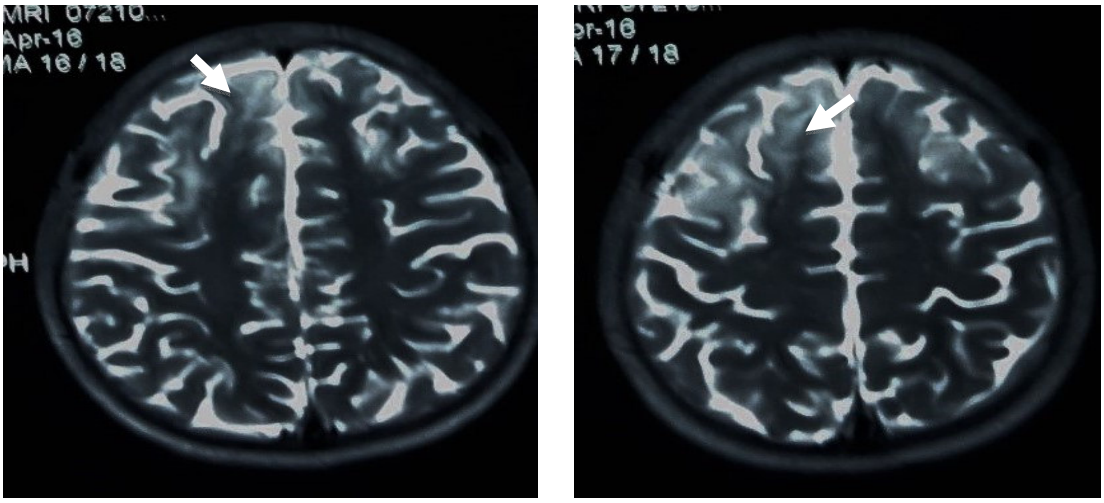


Figure-2: T2 axial images showing hyper intense signal (arrows) in cortical gray matter and subcortical white matter of bilateral frontal lobes and basal ganglia.

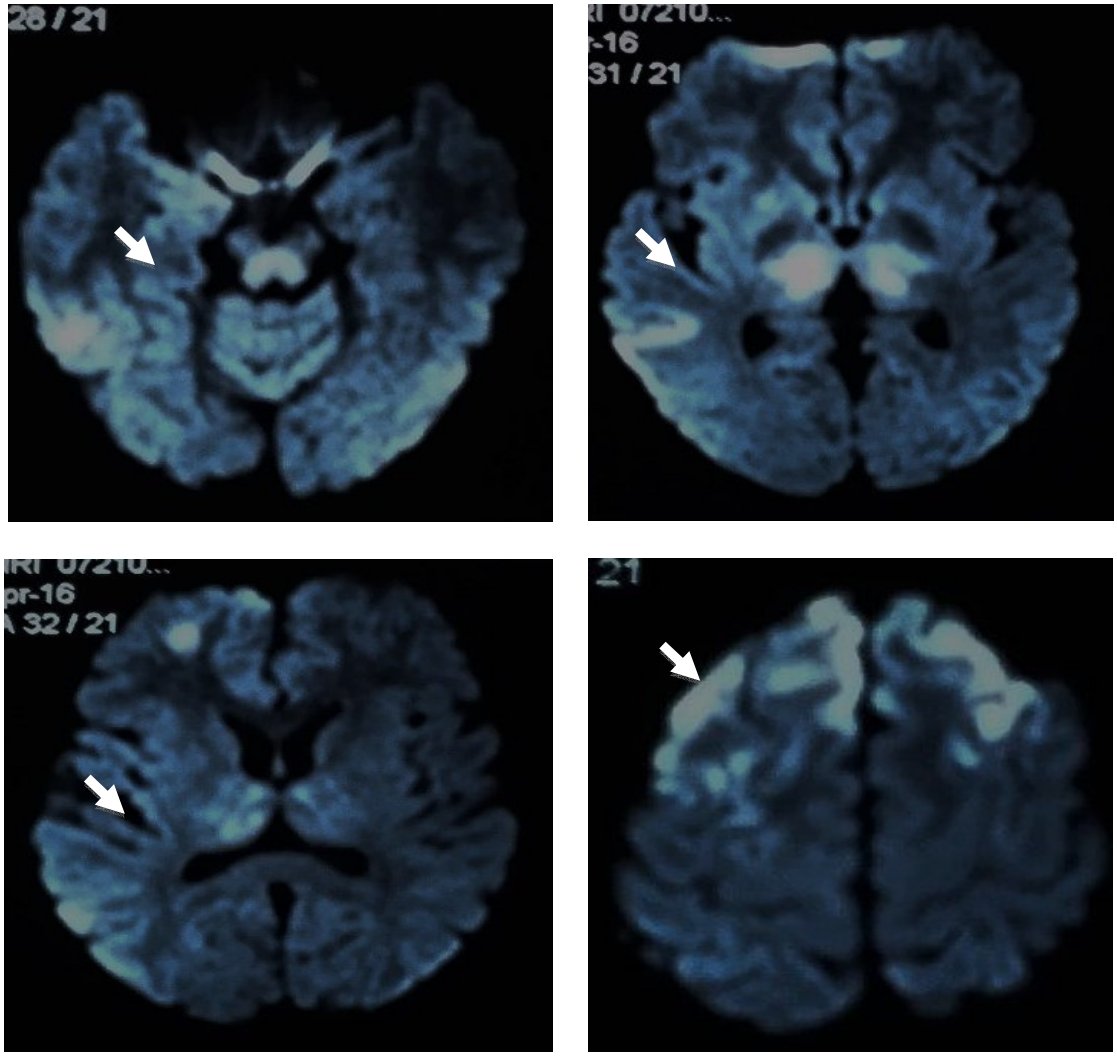


Figure-3: Diffusion weighted axial images showing hyper intense signal (arrows) in cortical gray matter and subcortical white matter of bilateral frontal lobes, basal ganglia, thalami and midbrain suggestive of diffusion restriction.

Discussion

Clinical presentation of Wilson Disease is mostly hepato, neuro-ocular, ranging from the asymptomatic to a fulminant variety with hepatitis, portal hypertension, protean neurological and psychiatric symptoms. Clinical presentation of Wilsons Disease is between 5 to 50 years [2].

However, early childhood Wilson disease usually presents with chronic liver disease or hemolytic anemia and neurological manifestations are rare before the age of ten years [1]. Girls are 3 times more likely than boys to present with acute hepatic failure.

Clinically evident liver disease may precede neurologic manifestations by as much as 10 yr. After 20 years of age, neurologic symptoms predominate [5]. Clinicians are well aware of the frequently described basal ganglia and brainstem abnormalities as well as cerebral atrophy in Wilsons Disease.

Diagnosis is based on clinical evaluation along with biochemical and neuroimaging confirmation.

Biochemical studies may show a low serum ceruloplasmin level (<20 mg/ dl) and increased urinary copper excretion (more than >100 µg copper per 24 hours). Hepatic copper estimation, of more than 250 g/g of dry tissue (Normal 15-55 µg/g) is the most definitive method of diagnosis [2].

In a large study of MRI Brain in 100 patients with WD, the salient findings included: Atrophy of the cerebrum (70%), brainstem (66%) and cerebellum (52%), signal abnormalities in putamen (72%), caudate (61%), thalami (58%), midbrain (49%), pons (20%), cerebral white matter (25%), cortex (9%), medulla (12%) and cerebellum (10%). The characteristic face of giant panda' sign was noted in 12% and feature of central pontine myelinolysis was noted in 7% and bright claustral sign in 4% of patients [6]. So, the involvement of basal ganglia and midbrain is common finding in Wilson disease, however involvement of gray and white matter is a very rare finding as in index case, which signifies copper toxicosis.

The possible hypothesis for this signal changes are combination of demyelination, spongy degeneration, softening and cavitation [3, 4]. It has been observed that patients with white matter lesions on MRI may have poor response to de- coppering therapy [7] [8].

Conclusion

- Index case presented with neurological manifestation of WD without any liver involvement at an earlier age.
- Cranial MRI showed a rare involvement of gray and white matter, which is reported rarely.
- As clinicians we are well aware of the common MRI picture.
- It is essential to also know the involvement of gray and white matter in Wilson disease indicates poor prognosis, which is less responsive to de-coppering therapy.

List of abbreviations

WD- Wilson disease

ATP- Adenosine triphosphate

KF – Kayser –Fleischer

MRI- Magnetic resonance imaging

WBC- White blood count

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References

1. Taly A B, Prashanth L K, Sinha S. Wilson's disease: An Indian perspective. Neurol India 2009;57(5):528-40. DOI:10.4103/0028-3886.57789.

2. El-Youssef M. Wilson disease. Mayo Clin Proc. 2003 Sep;78(9):1126-36.DOI:10.1016/S0025-6196(11). 62937-6

3. Deiss A. Cecil textbook of Medicine. 20th ed. Singapore: Harcourt Asia Pte Ltd; 1999. 1131-2.

4. van Wassenaer-van Hall HN, van den Heuvel AG, Jansen GH, Hoogenraad TU, Mali WP. Cranial MR in Wilson Disease: Abnormal white matter in extra pyramidal and pyramidal tract. Am J Neuroradiol 1995;16(10):2021-7.

5.van Wassenaervan Hall HN, vandeneuvel AG, Algra A, Hoogenraad TU, Mali WP. Wilson Disease:Findings at MR imaging and CT of the Brain with clinical correlation. Radiology 1996; 198(2): 531-36. DOI:10. 1148/radiology.198.2.8596862.

6. Prashanth LK, Taly AB, Sinha S, Ravishankar S, Arunodaya GR, Vasudev MK, et al. Prognostic factors in patients presenting with severe neurological forms of Wilson's disease. QJM 2005;98 (8):557-63. DOI:10. 1093/qjmed/hci095.

7. Aikath D, Gupta A, Chattopadhyay I, Hashmi MA, Gangopadhyay PK, Das SK, *et al*. Subcortical white matter abnormalities related to drug resistance in Wilson disease. Neurology 2006;67(5):878-80.

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